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# PROGRESSIVE MEDICINE.

A QUARTERLY DIGEST OF ADVANCES, DISCOVERIES,  
AND IMPROVEMENTS

IN THE

MEDICAL AND SURGICAL SCIENCES.

EDITED BY

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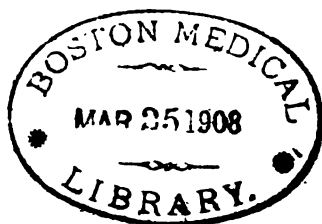
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PANCREAS—DISEASES OF THE KIDNEYS—SURGERY OF THE EXTREMITIES,  
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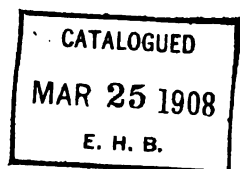
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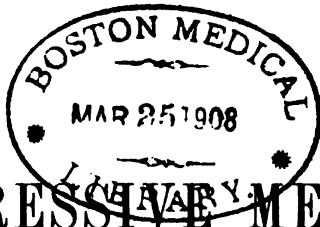
## CONTENTS OF VOLUME IV.

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	PAGE
DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER AND PANCREAS . . . . .	17
By J. DUTTON STEELE, M.D.	
DISEASES OF THE KIDNEYS . . . . .	113
By JOHN ROSE BRADFORD, M.D., F.R.C.P.	
SURGERY OF THE EXTREMITIES, FRACTURES, DISLOCA- TIONS, TUMORS, SURGERY OF JOINTS, SHOCK, ANES- THESIA, AND INFECTIONS . . . . .	135
By JOSEPH C. BLOODGOOD, M.D.	
GENITO-URINARY DISEASES . . . . .	227
By WILLIAM T. BELFIELD, M.D.	
PRACTICAL THERAPEUTIC REFERENDUM . . . . .	259
By H. R. M. LANDIS, M.D.	
INDEX . . . . .	329







# PROGRESSIVE MEDICINE.

DECEMBER, 1907.

## DISEASES OF THE DIGESTIVE TRACT AND ALLIED ORGANS, THE LIVER AND PANCREAS.

By J. DUTTON STEELE, M.D.

### THE STOMACH.

**Normal Physiology of the Digestive Tract.** HORMONE (derived from the Greek, *ὀρμω*, to arouse or to stimulate) is a word coined by Starling to furnish a name for that group of substances which are formed in one organ or tissue for the purpose of stimulating some other more or less remote organ to which it is carried by the blood stream. It is thus to be distinguished from purely nervous stimulation. The best known example of a hormone is secretin, which is formed in the duodenal mucous membranes and is carried to the pancreas by the circulation.<sup>1</sup> Another example is the internal secretion of the pancreas, which stimulates the glycolytic ferment of the muscles.

Starling believes that the liver and intestinal mucosa are stimulated by hormones formed in other parts of the gastro-intestinal tract and comparable with secretin. Probably the fetus secretes hormones which stimulate the growth of the mammary glands, and the corpus luteum may produce hormones which affect menstruation and pregnancy.

The internal secretions of the testicle and ovary may be hormones; indeed, many of the so-called internal secretions are probably hormones, although not all of them.

I repeat, that hormones are circulatory and not nervous stimuli. They are also to be distinguished from the activating action of the various gastro-intestinal secretions upon each other.

OBSERVATIONS UPON THE MECHANISM OF THE STOMACH. Scheunert<sup>2</sup> investigated the amount of mingling of different foods in the stomach.

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1905.

<sup>2</sup> Pflüger's Arch. f. d. gesammte Physiol., 1906, Band cxiv, p. 64.

He fed horses upon oats and hay, part of which was colored with gentian blue and part with Bordeaux red. The animals were killed after periods of one-half, one, three, and six hours, and the stomach was frozen in situ. It was found that the different material lay in the stomach in layers even after an hour's time. He never found that the different foods were mixed. The character of the layers depended upon the shape of the stomach, its position in the abdomen, and especially upon outside pressure. The physical character of the food and the amount of chewing influenced the amount of intermingling.

Sick<sup>1</sup> performed part of his experiments upon animals which were killed at the end of an hour. He hardened the stomachs in formalin solution. He found that there was a sharply defined distinction between the cardiac and pyloric portions. The pyloric part never showed any material change in shape from that seen in a fasting stomach, while the fundus showed, after the injection of food, an active relaxation of its musculature. He considers that this is reflex and may be considered an active diastole of the gastric muscle.

When he measured the pressure in a normal stomach by the method used by Moritz, Sick found characteristic and different pressures in each portion. In decreased gastric motility the pressure in both portions falls to the minimum.

In another series of observations Sick used the *x*-rays, and found that there was a distinct stratification of the gastric contents.

In studies upon the gastric secretion Sick found that the chyme was entirely different in its chemical and physical characteristics in the different portions of the stomach. He believes, from the result of his investigations, that the pyloric mucous membrane is rich in pepsin and rennin secretion, but produced little or no HCl. In pathological lowering of secretion the difference between the secretion of the two portions entirely disappeared.

INTRAGASTRIC TENSION, INTRA-INTESTINAL TENSION, AND THE TENSION IN AEROPHAGIA; EXPERIMENTAL AND CLINICAL OBSERVATIONS. Dobrovici<sup>2</sup> has measured the pressure in various parts of the intestinal tract by means of a water manometer. His experiments were carried out both upon dogs and men under normal conditions and in aërophagia. In dogs he found a positive pressure of 1 cm. inside of the stomach, which changed upon respiration as the intrathoracic pressure changed.

The pylorus resisted a pressure of 20 cm. before opening. At a pressure of more than this gas escaped slowly into the bowel, when the tension immediately rose, while that of the stomach sank to normal. Liquids passed the pylorus at much lower pressure than gas, and a

<sup>1</sup> Deutsch. Arch. f. klin. Medizin, 1906, Band lxxxviii, p. 169.

<sup>2</sup> Thèse de Paris.

mixture of gas and fluid passed out still more easily. In the empty duodenum the intestinal pressure was 8 cm. The pressure was constant and was not affected by respiration, differing in this respect from the stomach. The pressure in the jejunum was the same as that in the duodenum. The pressure in the upper bowel was somewhat higher than in the portal circulation, where the tension was 7 cm. of water. The pylorus resisted a pressure of 40 cm. in the duodenum, and even then allowed no air to pass up into the stomach. The ileocecal valve also resisted a pressure of 40 cm. in the colon and allowed nothing to pass upward. The pressure in the middle of the large bowel was 1 cm. The ileocecal valve never allowed any regurgitation under any pressure.

In healthy men Dobrovici found air always present in the stomach. The intragastric pressure was positive and reached 4 to 5 cm. as an average. During respiration it rose and fell 3 to 4 cm., being higher during inspiration and lower during expiration. An hour after eating a meal the pressure rose to 10 to 12 cm. and every five to seven minutes muscular contractions occurred, lasting for one to two minutes, during which the pressure rose often to 20 cm.

The maximum intragastric pressure that could be obtained by inflating a healthy stomach varied with different persons. In general a pressure of 15 to 20 c.c. can be reached without any disagreeable sensations.

According to Dobrovici,<sup>1</sup> *aërophagia* in the unconscious and involuntary swallowing of air occurs, usually in the course of neuroses of the stomach. The study of such cases from the side of the gastric tension led Dobrovici to the following conclusions:

1. In the fasting stomach of such cases the tension was normal.
2. During eating the swallowed air raised the pressure above the normal. He recognizes two different forms of the condition: (a) The majority show considerable hyperesthesia of the stomach when the organ is distended with swallowed air, and this produces quick emptying of the stomach by belching. (b) In the other less frequent variety there is no pain felt in the stomach, and the air remains until it passes into the bowel; so that the latter is overdistended and often shows an internal pressure of 20 to 25 cm. of water. This tympany can exist for a long time.<sup>2</sup>

Dobrovici reports a case of *aërophagia* which had cardiac and thoracic symptoms suggesting nocturnal asthma and sometimes angina.

**A FAT-SPLITTING FERMENT IN THE GASTRIC JUICE.** Heinsheimer<sup>3</sup> has made several series of investigations concerning the fat-splitting ferment of the stomach. He has used the method of Volhard, who employs an emulsion of the yolk of egg. This is mixed with the gastric

<sup>1</sup> *PROGRESSIVE MEDICINE*, December, 1904.

<sup>2</sup> *Ibid.*, loc. cit.

<sup>3</sup> *Deutsche med. Wochenschrift*, 1906, Nr. 30; *Arbeiten a. d. path., Inst. zu Berlin*, 1906, p. 506.

juice, digested with a few drops of toluol for twelve to twenty-four hours, and extracted with ether and alcohol. The acidity of the ethereal extract is then determined. All observations in vitro are controlled by boiled gastric juice. The experimental observations were carried on in dogs with Pawlow fistulæ. His experiments showed that 25 per cent. of the fat was split in the first hour in the dog's stomach. When the experiment was carried out with human gastric juice in vitro the same result was obtained in acid, neutral, and alkaline mediums, but best in an acid one.

The fat-splitting power disappeared from the gastric secretion in cases of atrophy of the mucous membranes and in cancer of the fundus, indicating that the fat-splitting ferment was secreted in the stomach, and probably from the fundus. It was not due to regurgitation of pancreatic juice. The lipase is present only in fresh gastric juice, for when the secretion from the stomach is kept for a short time, even on ice, the lipase disappears.

London's investigations tend to contradict the work of Heinsheimer. He<sup>1</sup> has studied the question of a gastrolipase in a dog with a pyloric fistula of such a character that regurgitation of bile, pancreatic and intestinal secretion, was prevented. He found that in this form of fistula there was but 2.7 to 5.6 per cent. of splitting in an emulsion of fat, while in ordinary fistulæ he had always observed 17 to 23 per cent. of splitting. He believes that this indicates that the splitting which occurs in the stomach is due not to a gastric ferment but to a regurgitation of intestinal juices. It seems possible that both observers are right to some extent and that there is a lipase secreted in the fundus of the stomach, but that some of the fat splitting observed in the stomach is due to the secretion of organs lower down which has regurgitated through the pylorus.<sup>2</sup>

EXPERIMENTAL OBSERVATIONS UPON THE SECRETIONS OF GASTRIC JUICE IN THE HUMAN BEING. Bickel<sup>3</sup> has reproduced to some extent Pawlow's experiments upon dogs in the human being. The subject had both esophageal and gastric fistulæ which were made because of a stricture of the esophagus. In sham feeding experiments<sup>4</sup> Bickel found that secretions of gastric juice in the human occurred with two kinds of stimuli: (1) Those which arise through direct contact with the mucous membrane. (2) Those arising in the sense organs, or the so-called "appetite juice" of Pawlow.

This latter secretion follows stimulation of the taste and smell organs especially. Under such stimuli, a secretion could be produced in the gastric mucous membrane at rest and a secretion already established was increased. The "appetite juice" in sham feeding behaved in human

<sup>1</sup> *Zeitsch. f. physiol. Chemie.*, 1906, Band 1, p. 125.

<sup>2</sup> *PROGRESSIVE MEDICINE*, December, 1906.

<sup>3</sup> *Deutsche. med. Wochenschrift*, 1906, xxxii, Nr. 33.

<sup>4</sup> *PROGRESSIVE MEDICINE*, December, 1903

beings much as it did in dogs. The secretion produced contained a high percentage of HCl and ferments and, moreover, was about constant in its total acidity. Bickel believes that this last observation indicates that the percentage of acid in the human gastric juice is nearly constant, but that the quantity of secretion can vary considerably. The quantity is determined by nervous stimuli, by the water and chlorine content of the blood and by the quantity of juice required by each sort of food. But while the quantity of secretion is extraordinarily variable and adaptable, its percentage composition is very constant. He believes that the so-called hyperacidity is produced not by actual concentration of the acid, but to a combination of a hypersecretion and some disturbance of gastric motility, especially a hypermotility, and that an increase in the actual percentage of HCl probably does not occur. This is not a new observation, but has been suggested by several writers.

**DIGESTION AND ABSORPTIONS IN THE DIFFERENT PORTIONS OF THE INTESTINE.** Abderhalden, Kantzsch, and London<sup>1</sup> have studied protein digestion in dogs by making fistulæ in the different parts of the gastro-intestinal tract and then feeding the dogs with lean meat. They investigated the amount of amino-acids and the products of digestion. They found the merest trace of amino-acids in the stomach and considerable amounts first in the duodenum. At the ileocecal valve the intestinal contents still contained amino-acids—that is, absorption was not complete in the small intestine.

London and Polowzowa<sup>2</sup> have studied the albumin and starch digestion by the same methods in the different divisions of the gastro-intestinal tract. The material was obtained through fistulæ, filtered and analyzed. The results were naturally very different at the different levels. In general the amount of digestion can be stated as follows: The stomach digested one-third of the total solids ingested, the duodenum one-half to three-fifths, jejunum one-tenth, the upper ileum one-twelfth, and the lower portion of the small intestine one-fiftieth. Naturally, the digestion of albumin differed from that of starch at different levels. In studying the absorption they found that no albumin or carbohydrates were absorbed from the stomach. In the duodenum one-sixth was absorbed, one-fifth in the jejunum, three-tenths in the upper ileum, and then one-fourth through the part of the bowel below. The absorption went on with equal intensity in all parts of the small intestine, while digestion was most intense in the stomach and diminished gradually in the smaller intestine.

**THE NATURAL INHIBITION OF THE GASTRIC JUICE.** Sailer and Farr<sup>3</sup> have carried out a series of experiments chiefly outside the body in order to throw additional light upon the vexed question of inhibition

<sup>1</sup> Zeitsch. f. physiol. Chemie, 1906, Band 1, p. 125.

<sup>2</sup> Ibid., 1906, Band xlix, 328.

<sup>3</sup> American Journal of the Medical Sciences, January, 1907.

of gastric digestion. That peptic digestion is inhibited after a certain period is certain. What the character of the inhibitory agent is remains uncertain. Danielewsky claims that it is a substance present in the gastric secretion which he calls antipepsin. Other observers have claimed an inhibitory power (1) for various foods, (2) for the products of digestion, and (3) for the various mineral constituents of the chyme.

Sailer and Farr have carried out their experiments with artificial pepsin and HCl mixtures outside the stomach. It should be remembered that the results obtained apply to the inhibition of the pepsin in the gastric juice after it has been secreted and has nothing to do with the activity of the gastric secretion. It means that peptic action is arrested in the solution by the various substances experimented with. They conclude that while albumins do not inhibit, albumoses have a strong inhibiting effect. Under normal conditions this inhibition is probably not active in the stomach, although under abnormal conditions, particularly in cases of retention, it may be a serious factor. Gelatin has a distinct inhibitory effect. Of the sugars maltose appears to exert the strongest inhibition and lactose none at all. It is not probable that this inhibition ordinarily plays an important role in gastric digestion. Hydrocarbons apparently do not inhibit pepsin, at least when they are added to the gastric contents.

**Morbid Physiology of the Digestive Tract.** INHIBITION OF PEPTIC ACTION BY ARTIFICIAL MEANS. The second part of the paper by Sailer and Farr<sup>1</sup> is concerned with the effect of various antiseptics employed in the preservation of foodstuffs. The controversy excited by the use of these substances has been exceedingly bitter, and, as is usually the case, experts have testified for both sides. In testing the effect of these preservatives reliance has hitherto been placed chiefly upon the effect produced by feeding foodstuffs treated with them to human beings or even to the lower animals for a considerable period of time. In some cases, very careful studies have also been made of the urine in order to determine whether it irritates the kidneys during elimination. Only a few attempts have been made to study the direct effect of these preservatives upon the digestive processes, and yet this would seem the most obvious thing to do, and the disturbance of digestion a most likely source of injury. It must not be forgotten that the mere inhibition or non-inhibition of peptic activity does not exhaust the capacity for harm of a particular preservative. Nor has the present series of investigations indicated what effect these substances have upon the proteolytic activity of the pancreatic secretion. The result of this part of their work may be summarized as follows:

Of the ordinary preservatives boric acid and borax may be regarded as without effect upon the peptic digestion.

<sup>1</sup> Loc. cit.

Formaldehyde and alcohol appear to inhibit gastric digestion only when in high concentration.

Salicylic acid has a distinct inhibitory effect even in very high dilutions. This would seem to suggest that its reckless use may cause considerable impairment of nutrition.

Benzoic acid, sodium benzoate, and sodium sulphite inhibit gastric digestion very strongly. Resorcin inhibits very slightly. Creosote inhibits strongly, even in high dilutions.

On the other hand, carbonate of guaiacol, probably on account of its extreme insolubility in acid solutions, appears to have no inhibitory effect whatever.

Their results are very interesting and important as well from a therapeutic as from a sociological standpoint. We all know that certain drugs "upset the stomach," but when we know definitely that gastric digestion is seriously disturbed by various substances which we use as medicines, we may be more cautious in the way in which we employ them.

**ATTEMPTS TO INCREASE PEPTIC ACTIVITY.** Sailer and Farr<sup>1</sup> attempted to discover some method of diminishing this inhibition of peptic digestion, or, in other words, to give their investigations a practical value in therapeutics. It is certain that pepsin is more active in dilute than in concentrated solutions, that is, there is less inhibition. Therefore, they tried the effect of dilution upon the digestive powers of the gastric contents. They discovered a very interesting fact. When a portion of a test meal was removed and the remainder of the gastric contents diluted, it was found that the diluted portion showed peptic activity greater than should have been expected in such a dilution. In some instances the peptic power of the diluted residue was as high as in the original test meal. For this apparent paradox two explanations can be offered:

The introduction of the diluting fluid either stimulated the secretion of the pepsin or else it converted some inactive form of pepsin into the active substance. In either case it caused a relatively great increase in the digestive power of the stomach contents. The therapeutic indication is not clear, but it would seem that the ingestion of large quantities of fluid in the late stage of digestion—that is, one or two hours after taking a meal—might considerably enhance the digestive activity of the stomach. Of course, it might have, in addition, some injurious effect either upon the motility of the stomach or upon the digestive activity of the intestine. Neither of these points has been determined.

If the mere ingestion of a considerable quantity of water can stimulate the production of active pepsin, there may be some method of stimulating the secretion of active pepsin in the gastric juice in cases in which it is ordinarily deficient or absent.

In doing this Sailer and Farr repeated the experiments of Jaworski,

<sup>1</sup> Loc. cit

and found that when a dilute solution of HCl was introduced into the fasting stomach of cases of achylia and also in one case of cancer of the stomach, distinct peptic digestion could be obtained in the fluid when removed after fifteen or thirty minutes, although previously test meals had failed to show any gastric secretion. The amount of acid used was 200 c.c. to 500 c.c. of a one-twentieth normal solution of HCl. These results agree strikingly with those of Bickel,<sup>1</sup> who found that HCl introduced into the fasting stomach of a dog which had chronic gastritis stimulated the HCl secreted, although it did not do so in normal dogs.

Whether the HCl serves merely to activate the pepsinogen, or serves also as a stimulant to its secretion, it is impossible to say. Presumably the latter, because in several of these cases the amount of acid already present in the gastric contents was sufficient to make digestion possible had there been any proteolytic ferment. The method, unfortunately, does not seem to be of value in distinguishing between carcinoma of the stomach and non-malignant achylia gastrica, although their investigations are still too few to enable them to speak with any certainty on this point. It does yield, however, a very distinct therapeutic indication, that is, that in cases of achylia gastrica the HCl should be administered before and not after meals. It should also be administered in sufficient strength and bulk to ensure active stimulation of the gastric mucous membrane. Of three cases of achylia, all of which have received it in this manner, two have been greatly benefited; the third had been brought in a fairly good condition by several years' treatment before it was employed.

**METT'S METHOD FOR ESTIMATING THE ACTIVITY OF PEPSIN.** Ever since the appearance on Pawlow's work on the digestive glands, the method of quantitatively estimating the activity of pepsin, as suggested by Mett, has been the standard. Sailer and Farr have done much work with the method and give a very good description of the technique, as follows:

"For filling the tubes we employ the whites of two or three eggs, well mixed to render the fluid as homogeneous as possible. Onuf<sup>2</sup> dries and redissolves the egg albumen, but this does not seem necessary to us, as we have been struck with the uniform results obtained with different lots of albumen. Thick-walled tubes of a caliber of 1 to 1.5 mm. are preferable to those of thinner walls and larger caliber, as they fracture more accurately and yield more uniform albumen columns. Sections of tubing, suited in length to the vessel to be employed in boiling, are filled with fluid egg-white by suction, and plugged with little balls of bread. When a sufficient number of tubes has been prepared they are dropped into a pan containing warm water, which is rapidly brought to the boiling point. This temperature should be maintained for five

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906.

<sup>2</sup> Journal of the American Medical Association, February 10, 1906.



minutes. Violent ebullition is to be avoided, as it may cause the formation of bubbles in the albumen or expel the latter altogether. The use of the boiling temperature simplifies the test without greatly impairing its accuracy.<sup>1</sup> After drying, the tubes are hermetically sealed with sealing wax or paraffin, and allowed to ripen for several days. Fine bubbles, which are seen at first, gradually disappear, and the tubes remain in good condition for a long time, being practically sterile. When needed for use these tube lengths are cut into sections, 2 to 3 cm. in length, with a triangular file; accurate fraction of both glass and egg-white is the rule. Portions showing retraction of the albumen or bubbles are rejected.

"For ordinary routine estimations we employ the undiluted gastric contents (15 c.c. or less), a dilution of one-fourth (4 c.c. to 12 c.c.), and a dilution of one-sixteenth (1 c.c. of contents to 15 c.c. of one-twentieth normal HCl). The latter dilution is the one used for quantitative comparisons. Two Mett tubes are placed in each dish (covered Stender dishes are most convenient), and the specimens allowed to digest in the incubator (37° C.) for twenty-four hours. At the end of this period the digested cylinders of egg albumen at each of the four ends are measured off, and the average reading calculated for each specimen. The relative amount of pepsin is then obtained by squaring the result, and, if desired, multiplying by the dilution, *e. g.*, by sixteen. By using Cowie's<sup>2</sup> table of squares even this mild mathematical exercise may be avoided. For making the measurements a pair of calipers with a vernier reading 0.1 mm. is very convenient. A lens is useful principally for reading the vernier. One end of the tube is placed against one jaw of the instrument, and then the other jaw is separated until its edge is visible through the opalescent edge of the albumen. If the tube is at all oblique the shortest side is taken, while if the albumen is uneven the highest point to which digestion has reached is measured. Air bubbles or separation of the albumen may lead to diminished or increased digestion, but the cause is usually evident."

To ascertain to what extent slight variations in the technique, such as are unavoidable in the ordinary clinical laboratory, affect the results of the test, they made several series of estimations, varying the conditions of the experiment in each case.

1. They found that minor differences in the caliber of the tubes did not affect the result appreciably.

2. Provided there was no putrefactive change, age did not seem to affect the tubes. Tubes that are too fresh are said to digest more rapidly than those that are ripe.

3. The variations in digestibility of albumen from different eggs,

<sup>1</sup> Sahli, *Diagnosis*, Philadelphia, 1905.

<sup>2</sup> *Physician and Surgeon*, 1904, vol. xxvi, p. 118.

variations in the time of digestion, and variations in the temperature of the incubator, had more or less effect upon the result.

In conclusion, they say: "On the whole, therefore, we have in Mett's method a sufficiently accurate measure of the activity of pepsin. Owing to the nature of pepsin, and the complex character of the inhibitory factors, very exact comparative estimations are not to be expected. With careful technique, however, the test is found to be surprisingly accurate in any given case. When the inhibitory factors are better understood it will be still more available, and itself offers the best means of unravelling the tangle. As a qualitative or, roughly, a quantitative method, it also has much to recommend it, since the tubes are easy to prepare, and may be more readily preserved than the customary disks of egg albumen."

**THE SAHLI DESMOID REACTION.** In my article of last year,<sup>1</sup> I called attention to the valuable work of Einhorn, by which he proved conclusively by clinical experiments that catgut can be digested in the bowel as well as in the stomach. This discovery, of course, renders the desmoid test of no value as a test of gastric function.

More recently, Saito<sup>2</sup> has shown experimentally how catgut is digested in the bowel and why the experiments of Sahli and Schmidt with pancreatic juice failed to digest catgut. In short, Sahli and Schmidt were led into error because they forgot that trypsin must be activated by intestinal secretion before it has marked proteolytic action. Without such activation it is to be expected that trypsin would not digest raw connective tissue. It is upon such false premises that many of the tests for gastric and intestinal functions are based. Besides the desmoid reaction, the presence of connective tissue in the stool as a sign of achylia gastrica, the nucleus test for lack of pancreatic juice, and so on. I believe that the digestive ferments of the stomach and intestines have more general power of digestion than the earlier observers supposed. Later investigations tend to show this and that there is no sharp line between the gastric and intestinal digestive processes. All this tends to show that we cannot expect to obtain the exact results in our tests of gastric and intestinal functions, but must be content with results in round numbers.

It is but justice to Sahli to quote his last paper upon the technique of his method. He<sup>3</sup> says that the failures in the use of his desmoid reaction are due to faulty technique. Many of the investigators have depended upon incorrect abstracts of his article, instead of reading the original paper.<sup>4</sup> He warns especially against the use of the desmoid bags made by Pohl, as they have been made incorrectly and without his sanction. It is recommended that each investigator should make his own bags strictly

<sup>1</sup> *PROGRESSIVE MEDICINE*, December, 1906, p. 26.

<sup>2</sup> *Berlin. klin. Wochenschrift.*, 1906, Nr. 40.

<sup>3</sup> *Deutsch. med. Wochenschrift*, 1906, xxxii, 1193.

<sup>4</sup> *Correspondenzblatt f. Schweizer Aerzte*, 1905, xxxv, Nrs. 8 und 9.

according to the instructions contained in the original paper. I doubt, however, whether even such care in the details of the method can render it of any practical value in the light of the work of Einhorn and Saito.

**THE PHYSIOLOGY OF VOMITING.** Volenti<sup>1</sup> has proved by experiments upon animals that when the isthmus of the fauces, pharynx, and upper segment of the esophagus is thoroughly anesthetized with cocaine, emetics acting centrally (apomorphine) fail to produce vomiting. Also emetics that act locally (tartar emetic and copper sulphate) produce their effect more slowly than usual, and sometimes not for several hours, that is, after the effect of the cocaine has worn off. When apomorphine is given under these circumstances the ordinary symptoms occur, namely, the salivation, belching, etc., but not the slightest particle of gastric contents is ejected. The fact that the objective symptoms accompanying vomiting occur without the ejection of food suggests that there is a nervous mechanism in the mucous membrane of the pharynx and esophagus that controls the sphincter muscle of the cardia.

Volenti presents several other facts that appear to support this view. He says that when the throat of a man is thoroughly cocaineized a sound meets considerable resistance at the cardia and can be pushed into the stomach only by the use of considerable force, whereas in the same patient without cocaineization the sound passes immediately into the stomach. Also, it is well known that tickling of the fauces will produce vomiting. The mechanism of the reflex is not known.

**SUBJECTIVE DISTURBANCE OF TASTE.** Sternberg<sup>2</sup> describes the case of a patient who experienced a continuous sweet taste in his mouth, which bore no relation to food and was continuous day and night. It was not influenced by acid foods. The saliva tasted sweet to the patient, although to other individuals it did not seem so. The application of an acid solution to the tongue produced a loss of taste for a time and then the former sweet taste returned. Prolonged washing of the mouth with the acid solution caused a bitter taste. Cocaine and ethereal oil had no effect. Subcutaneous injections of saccharin and the ammonia salts of saccharin increased the glycogeusia. Injections of lactate of quinine and of bimuriate of quinine had no effect at all.

**Movements of the Stomach and Intestines.** Pfaff and Nelson,<sup>3</sup> of Boston, have studied the movements of the stomach and intestines in the salt bath and by the x-rays. Their observations showed different results from those of Cannon<sup>4</sup> in that they never found the rhythmic segmentation movements in the intestines alternating with waves of peristalsis which Cannon described. On the other hand, they observed

<sup>1</sup> Centralblatt f. Physiologie, 1906, Band xx, Heft 14.

<sup>2</sup> Zeitsch. f. klin. Medizin, 1906, Band lix, Heft 5 und 6.

<sup>3</sup> Journal of American Medical Association, December 1, 1906.

<sup>4</sup> PROGRESSIVE MEDICINE, December, 1905.

irregular circular contraction of greater or less strength and almost no antiperistalsis which formed such an interesting and important part of Cannon's observations.

Pfaff and Nelson remark that it may be that the movements of the intestines which they observed may have been stimulated and altered by the salt in the bath.

EFFECTS OF DIFFERENT DRUGS UPON THE MOVEMENTS OF THE STOMACH AND INTESTINES. A very interesting part of Pfaff and Nelson's work is that in which they tried the effect of various drugs upon the intestines and stomach. The results of the experiments did not differ much whether they were performed with the animal in the salt bath or under the *x*-rays, but some of the control experiments showed that both methods changed the normal condition of the animal to some extent. Their results were as follows:

Croton oil, aloes, and podophyllin markedly increased the peristalsis of the whole digestive tract. With aloes the peristaltic waves began high in the stomach and made very deep constrictions, indicating that the organ was trying to expel its contents with considerable force. It is true the number of waves became decreased from four or five to two or three per minute.

This is a very interesting and important observation, because, if it can be proved true, it gives us two new drugs (aloes and podophyllin, for croton oil must be too irritating) with which we can influence and stimulate the stomach muscle.

In the discussion, Pfaff said that in his experience *physostigmine* was uncertain and unsatisfactory, which certainly agrees with my own experience. I shall try aloes and podophyllin in gastric atony with much interest.

Scammony, gamboge, elaterium, jalap, euonymin, and frangula, increased only slightly the peristalsis of the stomach, but increased the movements of the intestines very markedly. Scammony and gamboge produced diarrhea in the animals observed, but not in the controls.

Cascara increased the peristalsis of the intestines, but caused no defecation in the saline bath, but some under the *x*-rays. Tincture of rhubarb gave negative results, whereas the infusion of rhubarb increased peristalsis, caused defecation, which, however, was not diarrheic. The pharmacopeial preparation of senna gave negative results, but by making the infusion twice as strong, peristalsis was increased and defecation observed under the *x*-rays and in the saline bath. Purgation gave no results. Peristalsis was not increased, and there was no defecation even when the dose was increased to cause acute nephritis.

Of the salts, sodium sulphate increased peristalsis and produced watery discharges in all the animals experimented upon. The same results were obtained in the control experiments. Sodium phosphate acted similarly to sulphates, but it did not increase as markedly the peristalsis of the

stomach. Sodium chloride in small doses was negative as to increase of peristalsis; in larger doses it produced a toxic gastritis.

*Nux vomica* did not increase peristalsis either in rabbits or cats, whether observed under *x*-rays or kept in saline solution. Control animals also gave negative results with the drug as to defecation.

If they could explain the discrepancies between the experiments and the controls, the paper of Pfaff and his collaborator would be a very valuable addition to our knowledge of the pharmacology of some of our most important cathartics. As it is, their paper contains some very valuable therapeutic suggestions.

**The Action of Alcohol on the Stomach.** L. Kast<sup>1</sup> had the opportunity of making a series of experiments upon the human stomach through a gastric fistula, similar to those of Pawlow upon dogs. He found that alcohol stimulates secretion in the stomach to a greater extent than does water or common food substances. Not only the amount of the secretion, but also its duration, is increased. The results in man are practically the same as in the dog. Upon this latter animal, Kast has made more extensive experiments. In small amounts, and in a dilution under 10 per cent., ethyl alcohol does not increase the production of mucus. The stimulation extends only to the production of hydrochloric acid; the secretion of pepsin is not increased, and the digestive power of the gastric juice is diminished. In a dilution of 10 to 20 per cent. the secretion of gastric juice is still more actively stimulated, and at the same time the production of mucus is increased. In higher concentration the secretion time is shortened, and the formation of mucus is still more marked. Over 50 per cent. alcohol produces abundant mucous secretion, with short and relatively little hydrochloric-acid formation. Alcohol in strength above 70 per cent. has a corrosive action on the mucous membrane through its disintegrating effect upon albumin. Alcohol is, therefore, both a specific stimulant of hydrochloric-acid secretion and a local irritant of the mucous membrane. Its action is increased by the presence of other foods, such as bread and meat.

The stomach protects itself against the local irritating action of the alcohol, as it does against other irritants, by its peristaltic action, by absorption, by the production of diluting secretion, by the return of duodenal contents to the stomach, and especially by the secretion of protecting mucus. If these measures fail, a more or less severe inflammation of the mucous membrane results.

Regarding the injurious effects of alcohol, the author maintains that the occasional use of alcohol of less than 10 per cent. strength causes no harm. A strength over 20 per cent. is distinctly injurious to the empty stomach. A repeated use of the weaker dilutions leads to hypersecretion; later, a secondary catarrhal process is set up, which, finally, diminishes

<sup>1</sup> Arch. f. Verdauungskrankheiten, 1906, xii, Nr. 6.

the production of hydrochloric acid. The repeated ingestion of more concentrated alcohol leads to an irreparable chronic catarrh, with an abundant formation of mucus and a diminution in the production of hydrochloric acid. Absorption and motility of the stomach are stimulated by small quantities of diluted alcohol; higher concentrations have the opposite effect. The process of peptonization is not affected by dilutions of alcohol under 20 per cent., but is hindered by greater strengths.

Practically, the question of the effect of alcoholic beverages resolves itself into a question of the percentage of contained alcohol, but the effect is sometimes modified by the presence of other substances—such as sugar, dextrin, acids, glycerin, aromatic bitters, carbonic acid, extracts, higher alcohols, etc. Beer, white wine, and cider stimulate secretion to a greater extent than their alcoholic content would warrant, owing to a stimulating action of some of these substances. Red wine, owing to its tannic acid, has been known to diminish markedly the secretion of mucus in the declining stages of gastric catarrh. Sugar is known to diminish secretion, while carbonic acid favors it. There are no grounds for considering alcoholic beverages of less than 10 per cent. strength as harmful to the stomach. Those containing from 10 to 20 per cent. may be taken with food, as the percentage is thus reduced. Those containing over 20 per cent. cannot be considered harmless for the stomach.

The higher alcohols (butyl-, amyl-, and propyl-alcohol) are injurious to the gastric mucous membrane even in high dilutions. Brandy or whisky, when adulterated or containing much fusel oil, is, therefore, highly irritant to the stomach, even though taken only occasionally. Prolonged use leads to chronic inflammation with subacidity and abundant secretion of mucus. Unadulterated cognac and rum may be judged according to their alcoholic percentage.

The effect of alcohol in chronic catarrhal conditions of the stomach is somewhat different than under normal conditions. When the mucous membrane is in a state of chronic inflammation, alcohol has a less stimulating effect upon secretion, but increases to a greater extent the production of mucus. The habitual drinker requires alcohol regularly with his meals, because the other articles of food alone are not able to produce the same quantity of secretion which the stomach has accustomed itself to produce under the combined stimulation of alcohol and food.

Certain therapeutic conclusions may be drawn from these studies. Adulterated beverages and brandy are to be avoided in all cases. The stomachics and stronger spirits (*e. g.*, cognac) may be used in small quantities in cases of nervous depression when it becomes necessary to stimulate the appetite and secretion through the senses of taste and smell. When secretion is to be increased, in the absence of catarrhal conditions, wines, champagne, and cider may be recommended. A diet rich in fats requires a little wine to offset the diminution of secretion which they produce. Small quantities of the stronger wines are indicated in dimin-

ished motility. Beer is not to be employed in cases where there is disturbance of digestion. Hypersecretion is a contra-indication to the use of alcohol. The habitual use of alcoholic beverages as an article of diet is not to be recommended.

**The Morbid Physiology of Visceral Pain.** In my article of last year,<sup>1</sup> I reviewed at some length the work that has been done upon the morbid physiology of visceral pain. I pointed out the fact that it had been demonstrated that the abdominal viscera apparently had no sensation of their own. This statement is based upon the observations made upon the abdominal organs when the peritoneal cavity was opened under local anesthesia. It has been well known for some time that handling of the viscera and visceral peritoneum gives no pain unless traction is made upon the mesentery. Some doubt existed about the sensibility of the parietal peritoneum under such circumstances. Most observers think that it is sensitive, but Alexander Mackenzie, of Burley, holds that the parietal peritoneum itself is not sensitive, but that the subperitoneal connective tissue contains many sensory nerve filaments which makes it appear as if the pain originated in the peritoneum covering it.

The whole subject is extremely complicated and many theories have been advanced to explain how the pain of visceral disease originates. The one fact that started this controversy is the apparent insensibility of the abdominal organ when the abdomen is opened without general anesthesia.

A paper has recently appeared by Meltzer and Kast from the Rockefeller Institute<sup>2</sup> which apparently gives the keynote of the whole subject. It is an exceedingly valuable contribution to pathological physiology and is particularly important at the present time because it apparently gives the reason why we have been so puzzled as to the mechanism of abdominal pain. It appears that the whole discussion is based upon a false premise, and that the insensibility of the viscera during operation is not due to any lack of sensory nerves in the organ, but to some inhibitory process connected with the operation. This inhibitory agent appears to be the *cocaine* used to render the abdominal wall insensitive. Kast and Meltzer say that their experiments were carried out on dogs and cats, chiefly on the former. They employed various methods. The animals were well narcotized by ether, the abdomen opened, and immediately closed by temporary ligatures held together by clamps, and when the animal was partly out of anesthesia one or more of the clamps was taken off, thus permitting one or more of the intestinal coils to come out. These, as a rule, were kept moist and covered with towels saturated in warm saline solution. In other cases the entire body was kept in a saline bath of 39° C., the viscera being well covered with the warm salt solution. In still other animals the

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906, p. 93.

<sup>2</sup> Medical Record, December 29, 1906.

abdomen was opened under local cocaine anesthesia. The presence of sensation of pain was tested by pressing the organs with the fingers or with thumb forceps; by touching them with heated test tubes and by stimulation with the faradic current, and watching the reactions of the animal to these irritations. In all the stimulations great care was taken to avoid pulling the mesentery or touching the parietal peritoneum. They tested the various parts of the gastro-intestinal canal, the spleen, the kidneys, uterus, bladder, etc., but their present statement refers essentially to the gastro-intestinal canal, which they studied mostly.

All the experiments led up to one unmistakable result, which can be stated in a few words: The normal gastro-intestinal canal possesses the sensation of pain.

THE EFFECT OF SUBCUTANEOUS INJECTION OF COCAINE UPON THE ABDOMINAL VISCERA. However, the result alone was not satisfactory to them. They could not doubt for a moment that the actual observations of Lennander and other surgeons of high standing were perfectly correct. Why, then, this difference in the observations on man and the experiments on animals? Can there be such a fundamental difference between man and beasts? This is not very probable. But besides the difference in the subjects of the observations there was a difference in the conditions under which both observations were made. Lennander operated essentially under Schleich's infiltration anesthesia. Schleich's mixture, as Lennander employed it, consisted of 5 cg. of cocaine, 1 cg. of morphine, and 200 cg. of a normal salt solution. It seemed advisable to them, as a further step in their investigation, to study the possible effect of these ingredients upon the sensation of pain in the abdominal organs. They began with cocaine. The hitherto known effect of this drug is its local anesthetic effect. Lennander and other surgeons employed it for this very quality to deaden the pain during the incision, apparently without the remotest idea that the drug could also affect the sensibility of the distant isolated gut. Meltzer and Kast, nevertheless, decided to test it. After establishing the undoubted sensitiveness of the intestines, etc., 2 cg. of cocaine was injected into the tissues of the abdominal wall near the incision. They were then surprised, indeed, when they discovered that a short time after this injection all sensations disappeared from the intestines; even a very strong electrical stimulus no longer produced any reaction or effect. After thirty or forty minutes the sensation returned. Such observations were repeatedly made, and invariably with the same result.

Now, it could hardly be supposed that the cocaine crept over by capillarity or by some other manner to the intestines, and the observed anesthetic effect was a local one. Neither did it seem probable that the cocaine crept along the spinal nerves to the spinal cord and there came in contact with the pain-carrying nerve fibers from the intestines. The



most reasonable explanation was that the anesthetic effect was produced through the circulation. That would mean that cocaine had not only a local, but also a general anesthetic effect. This assumption was easily tested. The cocaine was now injected in parts distant from the abdominal cavity, in the thighs, arms, pectoral muscles, etc. The anesthetic effect upon the intestines was prompt and complete just the same.

In further experiments Meltzer and Kast established that 1 cg. was sufficient to bring out the desired effect, and this even in large dogs weighing 14 kilos.

They have, then, thus far established two facts: That the gastrointestinal canal possesses the sensation of pain, and that the subcutaneous or intramuscular injection of a comparatively small dose of cocaine is capable of abolishing this sensation for some time.

Of many investigations which are by no means finished only a few are mentioned which might have a practical bearing.

In the course of the investigations they exposed some intestinal coils to the drying effect of the air in order to bring on some degree of inflammation, and they then found that inflamed organs were distinctly more sensitive than normal ones; in fact, the sensitiveness is often greater than that of the skin. Now, Lennander and other surgical observers stated that in their experience also inflamed organs are completely anesthetic. They therefore tested the effect of cocaine upon the exaggerated sensitiveness of inflamed intestines and found that a somewhat larger dose of cocaine, say 3 cg., will completely abolish all sensations also from inflamed organs.

Another interesting point is the observation that the parietal peritoneum also loses its sensation by a hypodermic injection in any part of the body, but the anesthesia sets in here later and disappears earlier than in the internal organs. It is possible also that the degree of the anesthesia is lower, but they are not yet ready to make any positive assertion on that point.

There is a striking difference in the rapidity of the onset of the anesthesia between an intramuscular and a subcutaneous injection of the cocaine. When injected intramuscularly the anesthetic effect may be already complete after two or three minutes. Auer and one of the authors (Meltzer) reported some time ago on the rapidity of absorption from the muscular tissue of such drugs as curare, adrenalin, and morphine. Cocaine also belongs to this group.

An interesting and new fact is the observation which they made on the effect which the injection of a small dose of cocaine exerts upon the physical condition of the animal; it promptly quiets its excitement. The animals, which were very restless and howling, became perfectly quiet one or two minutes after the intramuscular injection of cocaine. They state that it may be claimed that the quietness was due to the abolition of the pain, and that they should have tested it on etherized but not operated

dogs. On awakening from the ether they howl just as much as operated animals; the howling is not due to pain, but to the ether intoxication. An injection of cocaine quiets them promptly. The physical effect seems to last longer than the anesthesia of internal organs. The injection has no narcotic effect, as the animal is apparently wide awake, and follows one with his eyes. The lid reflex is not abolished, but the cornea is anesthetic and the pupil is widely dilated. Whether the general sensibility is also reduced is a question that they are not yet ready to answer.

Their communication may be summed up as follows: The prevailing idea based upon exact surgical observations is that the abdominal organs, whether normal or inflamed, possess no sensation of pain. Meltzer and Kast have found in animal experimentation that the sense of pain is present in normal organs, and that it is considerably augmented in inflamed organs.

They found, further, that a subcutaneous or intramuscular injection of cocaine is capable of completely abolishing this sensation in normal as well as in inflamed organs.

They therefore offer the suggestion that the anesthesia of the internal abdominal organs observed by the surgeons was due to the use of cocaine.

They have finally found that the injection of a small dose of cocaine has a calming influence upon the excitation of the narcotized and operated animals.

**THE EFFECT OF EXTERNAL STIMULI UPON THE ABDOMINAL VISCERA.** It is obvious that both new observations with regard to the effect of cocaine are capable of practical application in medicine. I am in a position to know through the kindness of Dr. Meltzer that even this important discovery of the inhibitory action of cocaine given into the circulation probably is far from being the whole explanation of the inhibition of sensibility of the abdominal organs. The effect of any handling of an animal has a certain amount of inhibitory action. This is shown by the work done by Meltzer and Auer upon the peristaltic movements of the rabbit's cecum and their inhibition. They say:

The rabbit's cecum fills nearly one-half of the abdominal cavity and food has to get into it and leave it again by some moving force. Nevertheless, they find in the literature practically no statement on the movements of that organ. There is good reason for it. When the abdominal cavity of a rabbit is opened, the cecum, as a rule, shows no motion. They wish to report that, according to their observations, that organ exhibits well-marked and quite regular peristaltic movements; but these can be seen only in the normal animal. When a well-fed rabbit is fastened on its back on a holder and the hair of the abdomen is removed, as a rule, movements of the cecum can be seen sooner or later. The movements are well marked and characteristic in their appearance, and leave no doubt as to the organ in which they take place. They mention only a few details in this communication. As a rule, especially in well-fed

rabbits, the movements begin in the colon and travel toward the small gut, that is, they are antiperistaltic in character, but frequently at the end of an antiperistalsis, after only a short interval, the wave returns and runs from the small gut toward the colon; in other words, the antiperistalsis is often followed by a peristaltic wave.

Various influences suppress cecal peristalsis. Ether applied through the nose stops the movements, but they return in about a minute after the ether is removed. Pain, struggle, and fright stop the movements; but they soon return again. The most striking effect, however, is the one caused by opening the abdomen; the peristaltic movements, as a rule, disappear completely and permanently.

What is the cause of this complete abolition of the movements? The experimenters thought it might be due to the strong and perhaps continued pain which the laparotomy causes, but they found by cutting the spinal cord that this was not the case.

In the course of the latter series of experiments they made the observation that it was not necessary to open the peritoneal cavity to inhibit the movements. Cutting through the skin in the linea alba (in an animal with a cut cord) and dissecting it extensively from the muscles below was sufficient to abolish all cecal peristalsis. Furthermore, the movements returned as soon as the muscles were again covered by the skin, the cut edges of which were held together by clamps. It looked as if the cooling and drying due to the impact of the air upon the muscles above the cecum might have caused the suppression of the movements. But suspending the skin flaps and filling up the cavity above the muscles with warm physiological salt solution did not restore the cecal peristalsis. Furthermore, extensive dissection of the skin of the lower extremities also suppressed the movements. Finally, immersion of the lower half of the animal in a warm saline bath inhibited the movements for twenty minutes and longer. When the peristalsis was reestablished it could then again be inhibited by taking the animal from the bath. All the various conditions referred to could affect the cecum only reflexly and not directly.

These experiments led to the inevitable conclusion that the warm or cool bath, and the dissection of the skin over the abdomen and the lower extremities, were various forms of more or less effective stimuli which caused reflex inhibition of the cecal movements. The path of these reflexes could run only through the dorsal cord below the cut. This conclusion was then tested by the effect which the complete destruction of that part of the cord would have upon the inhibitory reflexes. Cecal peristalsis is frequently abolished by such an operation, but reappears sooner or later, and then is often more marked than before the destruction. It was found that after the destruction of the cord the peristalsis of the cecum could not be inhibited by baths, dissections, etc. It was thus established that the cecum is under the control of the inhibitory influences invested in the cord, which can be called into action by various, peripheral

stimulations. Such a stimulus may not be exposed to the air of a part of the body which is usually more or less covered.

Under these circumstances they believed they had reason to assume that the inhibitory influence of a laparotomy might be due also to such a stimulation and that it is in the nature of a reflex inhibition. But after further experimenting they found that opening of the abdomen, whether within a saline bath or not, unlike the other peripheral stimulations, inhibits greatly the cecal peristalsis; even after the destruction of the cord, only a few incomplete cecal waves appear after a laparotomy. They conclude that direct stimulation of the cecum caused by its exposure to abnormal conditions is capable of inhibiting its movements also directly. Laparotomy, therefore, abolishes the movements of the cecum by direct inhibition, assisted probably also by reflex inhibition.

Thus, we see from the work of Dr. Meltzer and his associates that Lennander and the rest were far from the truth when they assumed, because they found no sensibility of the abdominal viscera upon operation, that none existed. They forgot that they were causing disturbances of very complex and delicate mechanism by their manipulation and under such circumstances, could not argue from their observation what the normal sensory physiology of the viscera should be. I imagine that the researches of Dr. Meltzer and his associates will be even more far-reaching than they promise to be at present.

THE SIGNIFICANCE OF CUTANEOUS HYPERESTHESIA IN DISEASES OF THE GASTRO-INTESTINAL TRACT. I have repeatedly referred to the so-called Head zones in my articles in *PROGRESSIVE MEDICINE*.<sup>1</sup> The problem of the production of such areas of cutaneous hyperesthesia is closely connected with the mechanism of abdominal pain, which I have just discussed. The whole question is as yet far from settled and all that we can be sure of is that these zones of cutaneous hyperesthesia have some connection with diseases of the thoracic and abdominal viscera. A recent paper by Kast<sup>2</sup> gives a very good account of the present attitude of clinicians toward such phenomena.

In many patients the raising of a fold of skin and the exertion of moderately strong pressure on this fold will produce, within certain boundaries, disagreeable sensations or even pain. This abnormal sensitiveness of certain cutaneous regions occurs, aside from diseases of the nervous system, in patients who are suffering from diseases of internal organs. Since Head described this phenomenon in detail, these cutaneous regions have been termed Head's zones. In explaining their occurrence, it is assumed that a painful sensation, arising in an organ, is referred to that cutaneous region whose sensory nerves arise from the same spinal segment, which supplies nerves to the organ in question. A spinal segment which is repeatedly subjected to abnormal excitation from a diseased

<sup>1</sup> December, 1904, p. 98, and December, 1906, p. 97.

<sup>2</sup> Berlin. klin. Wochenschrift, 1906, Band xliii, Nr. 31, p. 1033.

organ, will in the course of time acquire a condition of increased irritability. As a result, sensory excitations coming from other parts of the same spinal segment will produce painful sensations that would not be perceived under normal conditions. It is, therefore, evident why the raising of a fold of skin within certain zones will produce pain if the corresponding internal organ is diseased. From a study of numerous cases Head was able to map out the characteristic zone for each internal organ. More recently, Willoughby carried this scheme into greater detail, and described relations between various zones and different parts of the same organ. For example, he assigned different regions of the skin to the various walls of the stomach, and to the different parts of the arch of the aorta.<sup>1</sup>

Kast has accumulated observations concerning the sensory relations of the abdomen. It must be borne in mind that all investigations of Head's zones offer the objection common to all subjective symptoms, namely, that of personal equation. The principle of the phenomenon, according to Head, rests upon a susceptibility of the skin to pain and thermal stimulus, but not to touch. Kast, however, believes that very many but not all cases exhibit a hypersensibility to touch as well as pain and heat. Investigation has shown that the cause for this disturbance of sensation does not lie in the skin itself, but elsewhere, most probably where the sensory cutaneous nerve fibers come into relation with the afferent sympathetic fibers from the diseased organs. This relation is found in the common spinal segment or the spinal ganglion. Here, under the influence of a diseased internal organ, certain changes occur, which render the cutaneous distribution of that segment more susceptible to painful sensations. There is, so to speak, a circumscribed neurasthenia.

Head's zones are found very frequently in disease of the viscera, but are by no means constant. No conclusions, therefore, can be drawn from their absence. An exception to this statement might be made in regard to *carcinoma of the stomach*. In 12 positive cases of gastric cancer Kast found the zones present in only one, and that was originally an esophageal cancer which had extended to the stomach. The same zones are found under such varied conditions, that no definite conclusion can be drawn from them as to the nature of the disease. Likewise, the attempts at localization of lesions by means of the situation of the zones, seem at present unpractical. When considered in connection with other symptoms, the phenomenon has a certain, though limited value. In obscure cases, when the organ giving rise to severe symptoms is in doubt, the finding of the hypersensitive zone may put the investigator on the right track. The level of the zone is a valuable indicator, in such cases, of the level of the affected organ. The more evident the zone is the more significant is its occurrence, especially in persons with healthy nervous systems.

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1904.

Certain errors must be guarded against. Above all, the hyperesthetic areas of hysteria must be excluded; also the hyperesthesia arising from neuritis, cerebral diseases, spinal tumors, epilepsy, disease of the vertebræ; also disturbances of sensation accompanying or following febrile diseases (typhoid fever, influenza), or accompanying uremia. Care must be taken also to distinguish the sensitive cutaneous areas covering bony protuberances in emaciated individuals.

**Intolerance of Fats.** Edsall<sup>1</sup> calls attention to the fact that in a certain class of cases there is a marked intolerance to fats. Sometimes this intolerance consists in poor fat digestion and absorption, but in a certain number of individuals there seems to be an inability to assimilate the fat after absorption. In other words, the trouble is metabolic and not digestive. There is no direct proof of such a disturbance of fat metabolism, but I believe that Edsall has good grounds in clinical observation for his statements that such a condition exists. As he says, it has been traditional with the laity for many years that fat is an exceedingly nutritious form of food.

In addition to this, in recent times, much wise emphasis has been laid by the medical profession upon the important part played by poor nutrition in a large number of diseases, and generous feeding has come to be an essential element of treatment in such cases. This almost always means the free use of foods that contain a relatively large proportion of fats—milk, cream, butter, eggs, olive oil, and the like.

None of us would object to such a rational and useful method of treatment. As Edsall says, the attitude of the profession in this regard is a distinct advance in the scientific treatment of chronic disease, but sufficient emphasis is not laid upon the fact that some patients are not able to handle fats in large amounts, and some, indeed, are not able to utilize them in normal amounts. Sufficient attention is not given to clinical methods by which one may attempt to determine whether a patient makes use of the fats that are given to him. Edsall says that open rebellion of the digestion against fatty foods is, of course, recognized, and any student can recite a few instances, such as fatty stools in icterus, pancreatic disease and extensive structural change of the intestinal wall, as examples of poor digestion and utilization of fats. At present, also, everyone is well acquainted with the fact that fat metabolism may go dangerously astray in some conditions, more especially in diabetes; but he does not believe that enough thought is given to the not uncommon, comparatively minor disturbances that seem to be dependent upon a greater or less inability to take fats, and are often first brought out by an attempt to push the fats of the diet, in the desire to improve general nutrition.

Poor fat digestion appears to be more common in infancy and early life, and on the average the young seem less able to digest fats than adults.

<sup>1</sup> Boston Medical and Surgical Journal, December 27, 1906, clv, No. 26.

It may be that they are equally less able to metabolize fats properly. Edsall refers to the hard, white stools, the so-called acholic stools without jaundice,<sup>1</sup> in which bile is present, as leukohydrobilirubin, or even as hydrobilirubin, but its characteristic color is obscured by the great excess of fat. The fat in such cases is in the form of calcium soaps.

In half-grown or older children, occasional unexplained but recurring attacks of vomiting of more or less severity can often be controlled if the fats are entirely or almost entirely cut from the diet. In such cases the amount of fat which causes the trouble is often not above the normal. In other words, such children appear to be unable to use the usual amounts of fats. On the other hand, sometimes it is found that such cases have been the subjects of an attempt to raise nutrition by forced feeding with fatty foods. The same disturbances, however, occur in adults as well as children, particularly in those that are receiving forced feeding.

Edsall has seen this fat intolerance in phthisical patients, as, indeed, all of us have who have had much to do with disorders of digestion. Some of these patients were referred to Edsall for gastric symptoms. They could not take milk, cream, or eggs without distress, and sometimes vomited them; but they could, without trouble, take skimmed milk and the white of eggs, showing that the fat was the disturbing factor.

Some adults cannot stand even a usual amount of fat. A certain number of persons have, for example, real distress after taking milk or eggs, even in moderation. With milk, this can sometimes be overcome by mere dilution or by modifying it in much the same manner as is done for infants by cereals, or cracker dust, or some such preparation. Quite as often where burning, regurgitation, or even vomiting occurs after taking milk, the symptoms can be controlled by substituting skimmed milk. In the case of eggs the yolk can be entirely removed at first, and then gradually given in graded quantities, so as to accustom the stomach to take the fat that egg-yolk contains.

Edsall calls attention to the fact that occasionally fat is not well tolerated in cases of *hyperacidity*. As a rule, fat is well borne in such cases, and is an important part of the so-called hyperacidity diet. However, as I have had occasion to point out,<sup>2</sup> it is probable that the benefit from a fat diet in hyperacidity comes as much from its effect upon nutrition as upon any inhibitory action that it exerts upon gastric secretion. Edsall has seen cases of hyperacidity which do not bear fats well, and whose symptoms are increased rather than helped by such a diet. In such cases, skimmed milk is a useful substitute for ordinary milk.

Edsall also emphasizes what has already been observed, that fat indigestion may cause constipation as well as diarrhea, particularly in children. We are well accustomed to seeing to the loose, yellow stools of a child who is taking too much fat; but it would be well to remember

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906.

<sup>2</sup> Ibid.

that constipation also may be due to the same error in diet. When fat constipates, the stools consist chiefly of calcium soaps, and are hard, dry, and white. The treatment is, of course, to reduce the fats of the diet.

Edsall refers, at some length, to metabolic difficulty in the assimilation of fats when fat digestion and absorption are nearly if not quite normal. As illustration of this, he records a short series of cases, one of which is so interesting that I quote his account of it:

A boy of ten years was referred to him because his breath was so offensive that his family, and especially his mother, who was devoted to him, but had very delicate susceptibilities, found it difficult to have him in intimate contact. In addition to this, the most apparent symptom, he was thin and sallow-looking, had dark rings under his eyes, was nervous and rather irritable, and tired easily. Edsall made a very careful general examination and studied his urine, stools, and blood, but found nothing abnormal, except the general look of ill-health and certain conditions of the urine that will be mentioned. He had no digestive symptoms, and a very competent specialist had just found the nose and throat normal. The mother said that the chief advice that had been given her as to treatment had been to get him better nourished, and hence she had been having him take milk, cream, and the like, freely, though not immoderately, for three years. During this time she thought that his general condition had grown rather worse than better; he had gained no weight, and his breath had undoubtedly grown worse.

Edsall attempted to demonstrate some evidence of intestinal putrefaction or fermentation not exhibited by the symptoms or the condition of the stools, and made estimations of the ethereal sulphates and volatile fatty acids of the urine and tested the urine for indican, and the distillate from the urine for phenol and acetone. He also estimated the total nitrogen and the ammonia nitrogen. The only abnormalities were a rather marked reaction for acetone, decidedly high volatile fatty acids, and possibly a somewhat high amount of ammonia for a child. These conditions were merely sufficient to emphasize slightly a suspicion that his difficulty was due to the fats of the diet, but they did not, of course, demonstrate it. However, Edsall removed the fats almost completely from his diet, gave him skimmed milk in generous amounts, replaced the fats by easily digested carbohydrates, and later, since he bore them well, gave him green vegetables freely. The only medication that he used was milk of magnesia, which he gave him temporarily because he had at first a little constipation, and because he thought the alkali was indicated.

The effect in this case was in most particulars exceedingly gratifying. His breath rapidly grew sweeter, and after two weeks, the mother said, she rarely noticed anything wrong with it. All offensiveness later disappeared and has not returned up to the present time—a period of two years.

In the other cases the offensive breath was noticed, though not nearly



in as marked a degree. The other symptoms were as in the case described.

Edsall calls attention to the fact—and I am sure we will all agree with him—that it is very difficult to accurately determine by a clinical examination of the stools as to the state of fat digestion and absorption. This is undoubtedly so, for finer points in diagnosis—such as the distinction between pancreatic disease and disease of the biliary passages with jaundice, and disease only of the biliary tract.<sup>1</sup> But, as Edsall says—and I wish to emphasize this point—much can be learned from a careful clinical examination of the stools, especially if this is done by a person experienced in such examinations.

I go farther in this respect than Edsall. He cites a case which is very interesting from several standpoints. He considers it an example of the fallacy of clinical examination of the stools.

The patient, a woman of forty-seven years, was admitted to the private ward of the University Hospital, under the care of Dr. Frazier, with a diagnosis of chronic appendicitis. She presented no signs of appendicitis, but had had digestive symptoms and loss of weight for several months, and an examination of her feces by myself (J. D. S.) had shown that they seemed to be composed almost entirely of fats and soaps. In the absence of jaundice this led to a strong suspicion that the patient had either severe pancreatic disease or extensive and grave disease of the intestine, probably the former. Her digestion of albumin was, however, apparently good. In order to determine the severity of the disturbance of fat absorption, Edsall estimated the total intake of fats throughout three days, and marked off the feces of this period with carmine. He then estimated the amount of fat and soaps in the feces, after drying and pulverizing, by means of extraction in the Soxhlet apparatus, the soaps having been converted into fatty acids by heating with acid alcohol.

She took during this time 142.24 gm. of fat, and passed in the feces 17.12 gm. of fat, including soaps. She had, then, rather poor absorption, but it was very much better than was indicated by the qualitative examination. Her feces were, as had been reported, composed in very large part (66.6 per cent.) of fat and soaps, but the total amount of feces (only 25.67 gm. of dry residue in three days) was so extremely small that the high relative amount of fat that they contained became of very much less importance than it had seemed to be, and really indicated only an extremely moderate grade of disturbance of absorption (only 12 per cent. of the intake having been passed in the feces) instead of the very severe grade that had been thought at first to be present.

While I agree with Edsall that an accurate quantitative examination of fecal fat cannot be made except by accurate methods, I venture to point out what seems to me to be a fallacy in his interpretation of the

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906

above result. The patient was constipated, the dried weight of the stools was low, and most of it (two-thirds) was fat. In other words, absorption was carried farther than is usual, as it is in most cases of constipation. But absorption was much more perfect for all other foods than fat; and so, while the actual amount of fecal fat was low, the actual amount of other food residue was relatively and actually very much lower.

To my mind this indicates that fat absorption was decidedly interfered with. Certainly the information to be derived from the clinical examination of the stools is too important to diminish in any degree our examinations of them, even if an accurate quantitative examination cannot be obtained.

**Some Facts about Digestive Ferments.** I have repeatedly taken occasion to call the attention of the readers of *PROGRESSIVE MEDICINE* to the irrational and ineffective manner in which the profession at large uses the digestive ferments therapeutically. I have pointed out that it is questionable whether digestion is ever aided by the artificial administration of *pepsin*. This is so for several reasons:

1. The pepsin in the gastric secretion is not nearly so often diminished as is the HCl. In very few conditions is achylia complete; probably in almost every case there is enough pepsinogen in the stomach to do all the work needed if it is activated by HCl.

2. The work of Pawlow has shown that the gastric secretion varies in composition and strength according to the sort of food ingested. The different digestive processes in the stomach especially are very complex, and it is doubtful whether we can hope for much help by the administration of small amounts of pepsin.

3. The work of Sailer and Farr, and of the Committee of the American Medical Association represented by Sollman, have shown that too often the preparation of ferments upon the market are almost if not entirely inert, either because they have degenerated after preparation or because for various reasons they are not active at the start.

Sollman has found that in alcoholic preparations the process of degeneration is decided, although not very rapid, so a freshly prepared alcohol solution of the ferments may be fairly active, but one that has been kept any length of time has almost certainly degenerated.

This is of great interest to the practising physician because so many of the proprietary preparations of pepsin and trypsin are alcoholic solutions, and are, as a rule, kept for some time.

Sollman says that aqueous solutions of the ferments also deteriorate very rapidly. The only liquid medium in which ferments can be preserved for any length of time is glycerin. In this connection it may be pointed out that the advantage of glycerins of pepsin made by extracting the mucous membrane directly with glycerin, over those made by dissolving dried, soluble pepsin in glycerin, is not very apparent. A carefully made glycerin extract would certainly be better than a cheap glycerin solution,

for the glycerin extraction precludes putrefactive changes; but the careful manufacturer of pepsin will have no difficulty in avoiding putrefaction. It may be true that the glycerin extract contains more milk-curdling ferment and is superior for the manufacturer of junket. For internal administration, however, this has no significance. Pepsin is used to digest proteids, and this power is possessed by the dry pepsin and by its solution in glycerin. If there are any therapeutic indications for other ingredients of the gastric juice (aside from the acid) they have not yet been formulated. As to the rennin, the most authoritative book dealing with ferments (Oppenheimer) speaks as follows:

"It does not appear to have any essential significance for the digestion of proteids. It is strikingly absent in the newborn, who consume much milk. Zuntz and Sternberg have even found that milk proteid coagulated by rennin is less easily digested than the original milk proteid, and attribute to this in part the relatively smaller availability of milk for adults, who produce more rennin."

Dry preparations of ferments if carefully protected will keep indefinitely.

**THE VALUE OF MIXTURES OF FERMENTS.** One of the most common mistakes made in prescribing ferments is to mix up several self-destroying ferments in the same preparation. It is well known that pepsin is destroyed quickly in an alkaline solution; trypsin is destroyed in a weak acid solution about as quickly; while the diastatic ferments are destroyed in an acid medium after a somewhat longer interval.

While the different experiments of Cannon,<sup>1</sup> Grützner,<sup>2</sup> and others have shown that ptyalin digestion goes on in the immobile cardiac portion of the stomach for a period of several hours, this probably does not apply to either pancreatic or diastatic ferments introduced as medicine, because such substances are not thoroughly enough mixed with the food when administered, but are given at such a stage of the meal that they lie upon the outside of the bolus of food in the stomach.

Moreover, pepsin destroys trypsin, and trypsin destroys pepsin. There are other elements involved, such as the imperfect activation of the trypsin, and so on.

It will be seen that mixture of ferments is irrational and ineffective. Consequently, when a proprietary preparation is advertised as containing all the digestive ferments in an active form, such claims are made either to appeal to ignorance of gastro-intestinal physiology in the practitioner, or from ignorance in the manufacturers themselves.

**Gastric Carcinoma.** **THE DIAGNOSIS OF GASTRIC CARCINOMA.** The importance of early diagnosis is so important that it would be well to keep the possibility of cancer before us when we start to examine any case in which the symptoms are consistent with early carcinoma.

<sup>1</sup> *PROGRESSIVE MEDICINE*, December, 1904.

<sup>2</sup> Pflüger's *Archiv f. d. ges. Physiologie*, 1905, cvi, p. 463.

*The Onset of the Symptoms.* The onset of the condition is one of the most important points in the early diagnosis. The history is usually that of a person in middle life who has previously had little or no trouble with digestion. As von Leube puts it, we have every reason to suspect carcinoma when we encounter a gastric disturbance which is resistant to treatment and progressively grows worse, particularly if this occurs in a person past middle life, who has always had a good stomach, has indulged his appetite freely, and tolerated all sorts of food.

As Küttner<sup>1</sup> says, the patient often ascribes the beginning of his illness to some indiscretion in diet. Sudden onsets are marked by vomiting and pain and are regarded as acute dyspepsia by the patient. On the other hand, the commencement of the trouble may be more gradual. The important point in the history is the causeless onset of an obstinate and progressive disturbance, especially if it occurs in a person past middle life. Rarely (in three of Küttner's cases) the disease first manifests itself in profuse hemorrhage from the stomach. When the onset is gradual the symptoms resemble closely those of gastric catarrh and the typical symptoms of cancer develop later. For this reason the idea has arisen that a cancer may develop from chronic gastritis.

Küttner says that in his very large experience he has seen only 3 or 4 cases in which he was sure that cancer had followed a prolonged catarrh of the stomach. But he is sure that the error is often made of mistaking early cancer for chronic gastritis. About the earliest reliable symptom of cancer is progressive loss of appetite, especially for meats, sometimes for other special forms of food as well. This loss of appetite is usually a very marked and early indication of gastric cancer. It sharply distinguishes cancer from ulcer when the appetite remains good. On the other hand, cancer cases sometimes retain a good appetite until the end.

*Predisposing Causes.* The age of the patient is not as an important symptom as was formerly thought. While, of course, cancer is more common in middle and late life, it occurs at all ages. E. Bernoulli<sup>2</sup> reports (1) a case of carcinoma of the sigmoid flexure at fifteen years of age, (2) a case of rectal carcinoma at seventeen years, and (3) a gastric carcinoma at eighteen years. He has collected from literature 12 cases of cancer of the stomach, 3 cases of carcinoma of the jejunum and ileum, 5 cases of malignant disease of the colon, 7 cases of sigmoid cancer, and 20 cases of rectal carcinoma, all occurring in the first twenty years of life. The disease was found at all ages, being even congenital in 2 cases. Carcinoma gelatinosum was the most frequent histological form, occurring in 16 out of the 50 cases. The symptomatology was usually the same as in cases of cancer in adults, although the peculiar cachexia seemed less common. The course was usually rather rapid. Heredity does not appear to play much of a part as a predisposing cause. Ewald found an

<sup>1</sup> Berlin. klin. Wochenschrift, 1906, xliii, Nrs. 25 und 26.

<sup>2</sup> Arch. f. Verdauungskrankheiten, 1907, xiii, p. 118.

hereditary tendency to cancer in 6 per cent. of 178 cases. Küttner is not disposed to regard injury as an important predisposing cause. It is hard to trace much connection between trauma and gastric cancer. Küttner suggests that an injury may call attention to symptoms which were previously overlooked.

**EARLY AND IMPORTANT SYMPTOMS.** Changes in nutrition and loss of weight when present are, of course, important corroborative evidence, but it must be remembered that such patients sometimes maintain a remarkable degree of nutrition even to the very end. Küttner refers to three laboring men who kept at work until almost the end of the disease. Pallor is a frequent symptom even without emaciation, and is probably due to loss of blood from small and repeated hemorrhages. Obstinate itching of the skin has been frequently observed in cases of gastric carcinoma, and Küttner regards it as a rather important symptom. Of very great importance are the evidences of putrefactive change in the stomach. This manifests itself as offensive belching or as disagreeable and putrefactive odor of the washing. Often this smell can be detected in pieces of necrosed tissue that lodge in the eye of the stomach tube before it is noticed elsewhere. Swelling of the supraclavicular glands upon the left side is a symptom, which is usually not of much assistance in an early diagnosis. It is quite rare for one thing and occurs usually only in the late stages of the disease. Even the presence of lactic acid is not conclusive because it also may occur in other conditions. The continued presence of definite amounts of lactic acid is strong evidence of cancer, but it is not an early symptom. Küttner agrees with Glassner that some information can be derived from the gastric contents as to the position of the tumor. Thus if a ferment and pepsin are both much diminished, the tumor is probably in the fundus. If rennin is present and pepsin is absent the tumor is at the pylorus.

The tryptophan reaction cannot be considered a reliable clinical method in the diagnosis of carcinoma.<sup>1</sup>

The motor function of the stomach is impaired in the great majority of cases of gastric cancer. This occurs not only when the tumor is at the pylorus, but also when it is at the fundus. On the other hand, it may happen, especially when the cancer is in the fundus, that motility may remain unaffected throughout the whole course of the disease. In examining the motor power of the stomach it is important to make the conditions identical at every test, and it is important that a fair-sized meal should be eaten upon the evening before the stomach is examined. A false idea of gastric motility has often been obtained by washing the fasting stomach in the morning, when only a small, liquid supper had been taken, and finding it empty. If a larger, solid meal had been eaten, retention would have been detected. The finding of *pvs* in the fasting stomach

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1904, p. 45.

is of the greatest diagnostic importance, since it cannot well be found under these circumstances in anything but cancer. The amount of pus may be very small, but it is always important. It may occur alone or mixed with blood, or mixed with mucus.

I have said enough in my last three articles upon the significance of occult blood in gastric carcinoma, so that a prolonged discussion of the value of the symptom need not be given here. I will say, however, that Küttner lays great importance upon the test. He says (and we must all agree) that the recognition of occult bleeding in the gastric contents or the feces alone is not conclusive, but must be considered in connection with the other symptoms, and then is very valuable evidence. The constant finding of blood has great differential value, especially in cases with retention and an acidity.

The continued absence of blood is an extremely valuable sign against cancer. Küttner has never been able to derive much help in diagnosis from examination of fragments of the gastric mucosa recovered from the stomach washing, because in his experience (and in mine) they can be obtained but rarely. When such fragments can be examined, of course the information obtained from them is important. Cohnheim considers the presence of protozoa and infusoria upon the surface of the gastric mucous membrane an important sign of cancer. They are, according to Cohnheim, a "relatively early" sign, since they can be found in the gastric contents before ulceration takes place. After putrefactive changes commence they quickly disappear.

The presence of "long bacilli," the so-called Oppler-Boas bacilli, have about the same significance as definite amounts of lactic acid. Very numerous bacilli are found generally in stagnant stomachs with the absence of HCl and the presence of lactic acid. Under these circumstances their presence suggests carcinoma, but this combination of conditions may, of course, exist in other gastric affections than cancer.

Single bacilli occur in normal stomachs, even in the presence of free HCl. Sarcinæ are not of great diagnostic significance, since their presence merely indicate stagnation and they may occur with free HCl. The urine is of little aid in diagnosis of gastric cancer. Albuminuria was rare in Küttner's cases, but the urine generally contained large amounts of indican and of Rosenbach's pigment. The repeated finding of albumosuria and a positive diazo reaction under some circumstances suggest cancer.

Rosenfeld suggested at one time that a high proportion of fatty acids in the urine indicate cancer, but this had not been confirmed.<sup>1</sup>

The *examination of the blood* gives no definite help in Küttner's experience, and I believe his opinion is borne out by the experience of most of us. While the secondary anemia of carcinoma ventriculi may

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1904, p. 48.

be so intense as to suggest pernicious anemia, in other cases this anemia is late in developing or unimportant in degree.

Baradoulin,<sup>1</sup> in 10 cases of cancer found *digestive leukocytosis* absent in all but 2 and in both of these HCl persisted. He found the same lack of digestive leukocytosis in cases of cancer in other parts of the body (breast, upper jaw, and rectum), and he thinks this is due to the irritation of the lymphatic glands by the cancer toxin, and so they cease to respond to such a mixed excitation as the process of digestion. In gastric ulcer digestive leukocytosis is always present.

*Continued Loss of Weight an Early Symptom.* Albu<sup>2</sup> says that the tests of the functional activity of the stomach do not give a certain index of cancer, but he believes that by close observation of the body weight, in connection with the patient's history, and by use of the functional tests, it is usually possible to make an early diagnosis provided one sees the patient in this stage, which is seldom.

He lays much stress upon the steady loss of weight, especially when the patient is at rest and upon such a diet that one would expect him to gain. The patient loses weight from the first, although the loss may be very slight. The symptom itself only means a disease with marked tissue changes, but in connection with the general clinical picture is very suggestive of cancer. He quotes several cases as an example, of which I give one:

The gastric symptoms had been present for about two months. There was pain which was independent of food, the appetite was good, and eating often relieved the pain. The test breakfast was expressed in the form of 20 c.c. of poorly digested material with some mucus and no free HCl. The total acidity was seven.

When the breakfast was repeated the digestion was worse. The patient was put upon a suitable but nutritious diet and was kept in bed. In one and one-half weeks he lost six and one-quarter pounds, although with the rest and diet he should have gained. An operation showed a cancer of the fundus about the size of a "crown piece." The tumor was probably the smallest ever diagnosticated during life.

*Solamon's Test for Gastric Cancer.* A. Zirkelbach<sup>3</sup> gives his results with the method of diagnosis first proposed by Solamon in 1903, which consists in determining the amount of albumin and nitrogen in the wash water from the empty stomach. The patient's stomach is washed out in the evening, and the following morning a test breakfast is given. This is withdrawn and tested for amounts of HCl, lactic acid, and total acidity. During the rest of the day a diet is given as free as possible from proteids. On this second evening thorough lavage is again practised, and the patient takes absolutely nothing until the next morning. Then the

<sup>1</sup> Russky Vrach, 1906, No. 28.

<sup>2</sup> Deutsch. med. Wochenschrift, December 27, 1906, xxxii, Nr. 52.

<sup>3</sup> Arch. f. Verdauungskrankheiten, 1906, Band xii, Nr. 6, p. 543.

stomach is washed out repeatedly with 400 c.c. normal salt solution, and the fluid is examined for albumin by Esbach's method, for nitrogen by Kjeldal's method. The mucin is first removed by acetic acid and the blood by sodium chloride and centrifugation, followed by filtration. The author found that the amount of albumin and nitrogen in the wash water is much greater in carcinoma than in any other gastric condition. In 100 c.c. of fluid the albumin varied from marked cloudiness to  $\frac{1}{4}$  per cent., while the nitrogen amounted to 30 to 80 mg. In all other sorts of cases the quantities were infinitesimal. Only ulcerative processes of the gastric mucous membrane will produce this condition. Whether round ulcer of the stomach will produce it as well as carcinoma has not been determined, owing to the dangers of lavage in gastric ulcer. The number of cases examined is still too small to state definitely what quantities of albumin and nitrogen indicate carcinoma with certainty. The test cannot be considered as pathognomonic when taken alone, but is of value in doubtful cases, when considered in conjunction with other symptoms.

*Advanced Symptoms.* The presence of a tumor if its connection with the stomach can be demonstrated is, of course, the surest sign of gastric carcinoma. If it cannot be palpated because of its situation, the diagnosis must rest upon the history and the other symptoms that have been mentioned. Küttner groups cases of cancer of the stomach as follows:

1. Carcinoma with good motor function: here HCl is generally absent. Lactic acid, long bacilli, and sarcinæ are absent.

2. Carcinoma with marked motor insufficiency. (a) Free HCl can be present; sarcinæ may be present. Lactic and long bacilli are absent. (b) Free HCl is absent, lactic acid is abundant, long bacilli are present, and sarcinæ are few and absent.

Class 1 is the hardest to diagnosticate, because such cases show no symptoms to distinguish them, especially in the early stages from certain benign gastric diseases, such as gastritis anacida or dilatation and certain gastric neuroses.

In uncertain cases the aids to diagnosis may be classified as follows:

1. Blood in the gastric contents and feces. Constant absence of blood is very much against the presence of a carcinoma.

2. The investigation of the fasting stomach. Constant presence of pus, especially if pus and mucus, or blood and pus, is in favor of cancer. Other conditions causing pus in the stomach are usually so obvious as to cause no confusion.

3. Fragments of the gastric mucosa in the gastric contents.

4. Amebæ and infusoriæ in the mucus of the fasting stomach.

5. The presence of albumin in the wash water of a fasting stomach. This is the so-called Solamon's test.<sup>1</sup>

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1904, p. 47.



6. The presence of a left-sided pleurisy, which Küttner has repeatedly observed in cases of cancer of the lesser curvature.

In the second division of Group 2 (2 b), the symptoms are usually so advanced as to have little doubt as to the diagnosis.

*The Occurrence of Fever in Carcinoma.* The first systematic observations upon this subject were made in Eichhorst's clinic by Freudweiler.<sup>1</sup> He found that 24.6 per cent. of 475 cases of carcinoma showed fever some time in the course of the disease.

Eichhorst gives the percentage as 27 in the latest edition of his textbook (1906).

Alfred Alexander,<sup>2</sup> writing from Albu's clinic in Berlin, adds several cases of his own, and draws some conclusions from his own material and that of Freudweiler.

Carcinoma of itself may cause fever, that is, in such cases the fever is not due to the presence of complications. The fever is atypical and irregular. Alexander reports four cases. In the first, chills and fever occurred abruptly every third or fourth day after the manner of malarial paroxysms. In the second case the fever was very irregular. For a day or so there would be fever, and then a ranging period of intermission. In the third case the temperature was remitting, with occasional malarial-like outbreaks. In the last case the fever was remitting, with occasional days of apyrexia.

A study of the distribution of the cancers which ran a febrile course showed that the great majority of them (108 of 117) were located in the gastro-intestinal tract; the remainder were scattered among the other common seats of cancer, though mostly in the abdomen.

The cause of the fever appears to be an auto-intoxication by products of tissue changes in the tumor mass. That it is not always the result of necrosis is shown by several cases which ran a febrile course with no ulceration, and vice versa. Fever is, however, more common in ulcerated cancers.

*The Diagnosis of Carcinomatous Ulcer.* The distinction between a simple ulcer and peptic ulcer and malignant degeneration is exceedingly difficult if not entirely impossible. The lack of improvement under the ordinary ulcer treatment, continuance of bleeding under a mixed diet, and intensity of the pain are symptoms in favor of cancer—but these cannot be considered decisive.

Audistère<sup>3</sup> says that the pain in *ulcus carcinomatosum* is usually very much more severe than in simple ulcer. A tumor may occur in simple ulcer, and, indeed, is not uncommon in this condition. A tumor that has shown no change for three years may be safely considered one formed by a simple ulcer.

<sup>1</sup> Deutsch. Arch. f. klin. Medizin, 1899, Band lxiv, p. 544.

<sup>2</sup> Deutsch. medicin. Wochenschrift, 1907, xxxiii, Nr. 5.

<sup>3</sup> De la degenerescence cancerreuse de l'ulcere de l'estomac, Paris, 1903.

Gluzinski's method<sup>1</sup> has not proved successful in Küttner's experience; consequently we have to acknowledge that we have no clinical method of detecting malignant change in a peptic ulcer. Indeed, often the surgeon cannot say definitely at operation by the gross appearance when cancer has commenced in the floor of an ulcer, and, what is more, sometimes the pathologist is at a loss to determine the same point microscopically.

Gastroscopic examination will probably not find much favor as a means of diagnosis in cancer on account of the danger of hemorrhage.

The method of diagnosis by blood-serum examinations of which much was hoped has not as yet proved of much value. Kelling has worked with the blood serum of fifteen cases of cancer (esophagus, stomach, and intestines) and obtained eight times a precipitin for egg albumen and twice for pig albumin. Fuld could not obtain a specific reaction in the blood serum of carcinoma cases with extract of the tumor.

*X-ray Diagnosis.* X-ray photography offers some hope that it will be of assistance in the diagnosis of cancer of the stomach. Holzknecht describes three points of diagnosis by means of the x-rays (after the administration of bismuth).

1. There are defects in the distribution of the bismuth over the tumor area owing probably to the crevasses in the tumor. This gives a certain area in the stomach an irregular appearance.
2. The shape of the stomach may be irregular and distorted.
3. With the fluoroscope there may be irregularities in the peristalsis of the stomach.

There is no doubt that a tumor can be recognized by means of the x-rays when it cannot be palpated. Küttner suggests that the x-rays may, however, not prove to be a very great aid in diagnosis of carcinoma of the stomach. He says it seems probable that if a tumor is present the condition will often be recognized by other means as well. He calls attention to a fact which should not be overlooked in considering operation, namely, that a small tumor may be very malignant.

**THE MEDICAL TREATMENT OF GASTRIC CARCINOMA.** Einhorn<sup>2</sup> suggests that we should always keep in mind the possibility of syphilis when we are treating a tumor of the stomach. In the great majority of cases antispecific treatment will have no effect, but it can do no harm, and 5 per cent. of such cases are specific. In the management of cancer he suggests the use of sedatives when necessary for the pain. The diet should be liquid in cases without marked stenosis, and may consist of eggs beaten in milk, or bouillon, oyster broth, calves-foot jelly, etc.

Two or three quarts of milk daily will materially aid nutrition. When there is no stenosis at all a semisolid diet is best. With marked stenosis

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1904, p. 47.

<sup>2</sup> Post-Graduate, December, 1906, xxi, p. 1192.

the patient will derive much comfort from a gastro-enterostomy. Einhorn advises the fluidextract of condurango bark to improve the appetite and as a stomachic. Chloral hydrate is an excellent sedative and antiseptic combined. It may be given in doses of 2 to 5 grains three or four times daily. Methylthionine hydrochloride seems to be of benefit in some cases and can do no harm.

Lavage is essential if much fermentation of the gastric contents is present. He has found the *x*-rays of little benefit. He has, however, used radium locally in malignant structure of the esophagus and cancer of the stomach with a decidedly beneficial effect.

**A CASE OF SECONDARY CARCINOMA OF THE STOMACH.** Castro<sup>1</sup> first systematically described secondary or metastatic gastric carcinoma. He found twenty-five cases in the literature. Only seven cases were in organs outside of the digestive tract. These were distributed as follows: Three times in the female breast, twice in the eye and tongue, once in the testicle, and once in the leg. The rest of the twenty-five cases were carcinomas of the esophagus. Naturally it is often very difficult, especially in cancer of the esophagus, to determine whether the secondary growth is an instance of true metastasis or whether it has arisen by continuity either directly or through affected lymphatic glands. This uncertainty was present in practically all of the cases of esophageal tumors, and if these are thrown out the undoubted cases are reduced to seven.

Joseph<sup>2</sup> adds another case. The man was a laborer, aged forty-eight years, with a primary carcinoma of the right breast, affecting the glands in the right axilla. The patient died six months after the operation, with quick emaciation and cachexia. There were metastases in the thoracic muscles, anterior mediastinum and its lymphatic glands, both pleuræ, lungs, sternum, tonsils, cervical lymph glands, liver, and left adrenal. There was, also, a cancer nodule near the pyloric end of the stomach 2 mm. in diameter. Microscopic examination showed that this was undoubtedly cancer.

Billroth gives the following conditions which must be fulfilled before it can be definitely stated that a growth in any structure is secondary:

1. The carcinoma must have a different structure from that usually seen in primary growths of that region.
2. The secondary growth must evidently be of the same structure as the primary.
3. The primary carcinoma must have general metastases.

In Joseph's case all the conditions are fulfilled; the secondary node in the stomach wall grew from the submucosa, and while it invaded the mucous membrane it had not broken through it.

**New Tests for Occult Blood.** Numerous papers have appeared during the past year dealing with the detection and clinical significance of occult

<sup>1</sup> Inaugural Dissertation, Berlin, 1890.

<sup>2</sup> Deutsch. med. Wochenschrift, 1907, xxxiii, Nr. 12.

blood in gastro-intestinal discharges. Various new and more delicate tests have been suggested, which I give below. Personally, I do not believe that we will gain much by refining our tests so as to get them very delicate. As more delicate tests for blood are devised, the danger of misinterpreting the positive findings will be greatly increased, and certainly they are great enough already.

As I have said elsewhere, I believe that the efforts of investigators should be turned toward determining the clinical significance of small and invisible hemorrhages from the gastro-intestinal tract, and not to devising methods of detecting minimal amounts of blood. Most successful methods of diagnosis in the gastro-intestinal tract and elsewhere deal in round numbers and do not attempt too great exactness. I believe that this will prove true of our tests for occult blood.

I referred to the benzidin test in my article of last year.<sup>1</sup>

Schlesinger and Holst<sup>2</sup> have modified the benzidin test by boiling the feces to exclude error from any oxidizing process which might give the same reaction. Their technique is as follows:

A concentrated solution of benzidin in glacial acetic acid is made fresh; a little benzidin and about 2 c.c. of the acid are shaken up together and set aside to dissolve. A piece of feces about the size of a bean is stirred into a test tube about one-fifth full of water. The tube is then plugged with cotton and the suspension of fecal matter is heated to boiling over a flame. It is advisable to have special test tubes for this work, 10 cm. long, so that there need be no fear of any accidental contamination with blood or iron. About 10 or 12 drops of the concentrated solution of benzidin are poured into another test tube and from 2.5 to 3 c.c. of a 3 per cent. solution of peroxide of hydrogen is added. This mixture is the reagent, and 1 or 2 drops of the boiled suspension of feces is then added to the reagent after shaking. In case of the presence of blood, the brownish fluid turns green or blue. The more blood present the more the tint inclines to blue, and the color reaction occurs very early, requiring only from a few seconds to two minutes or more with very minimal amounts of blood. The green or blue of the positive reaction turns to a dirty purple after from five to fifteen minutes. If there is no blood in the feces, the color of the brownish fluid remains unaltered even after twenty-four hours. The test as modified is much simpler than the others in vogue.

Einhorn has prepared a benzidin paper, which will simplify the test if experience shows that his method is reliable. It can be obtained from the firm of Eimer and Amend, New York. Boas<sup>3</sup> suggests another method, as follows:

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906.

<sup>2</sup> Deutsch. med. Wochenschrift, 1906, xxxii, Nr. 36.

<sup>3</sup> Centralblatt f. innere Medizin, 1906, xxvii, Nr. 24.

The material is treated in the usual way, with as little glacial acetic acid as possible (about 20 drops), and extracted with ether. To the ethereal extract 1 or 2 drops of a very dilute solution of paraphenyldiamin hydrochloride (1 to 200) are added. As the reaction occurs very slowly if at all in the presence of acid, 1 c.c. of one-half normal alcoholic solution of potassium hydroxide is added to the mixture, and then 10 to 15 drops of a 3 per cent. solution of hydrogen peroxide. There now appears immediately at the bottom of the test tube, after a little shaking, a characteristic olive-green color. Especially characteristic is the olive-green ring between the ether and the hydrogen peroxide layers, while the supernatant liquid shows a more or less intense violet color due to the action of the reagent. The green color is very evanescent and soon changes to a more or less deep dark violet, according to the amount of blood. In stools containing much bile or urobilin it is advisable to extract with alcohol-ether, according to the method of O. Schumm, before applying the blood test. In the absence of blood the green color either does not appear at all or only after long standing. Numerous control comparative trials of the new test and those previously used have shown completely concordant results.

Boas regards the method as easily applied and reliable.

Cowie<sup>1</sup> has modified the guaiac test slightly, as follows. I believe that he adds too much ether to obtain great delicacy:

1. All glassware must be chemically clean and perfectly dry.
2. To 1 gram of stool which has been softened, if necessary, by as few drops of water as possible, about 4 or 5 c.c. of glacial acetic acid are added and intimately mixed. This is best accomplished by rubbing up in a glass mortar.
3. To the above mixture add 30 c.c. of ether and allow to extract for several minutes, after thoroughly shaking or mixing.
4. To 1 or 2 c.c. of the extract, which is perfectly clear and can be decanted off, add an equal amount of distilled water and shake thoroughly.
5. To the resulting mixture add a few granules of powdered guaiac resin, an amount that will be held on the tip of a small knife-blade; this is allowed to dissolve and the tube is agitated thoroughly.
6. Thirty drops of old water-white, chemically pure turpentine are now added, and thoroughly mixed with the contents of the tube. Set aside against the light or in front of a white surface.

If blood is present to the amount of 1 mm. to 1 gm. of stool, a distinct light-blue color develops quickly in the upper half of the mixture, remains for a short time, and gradually disappears. Larger amounts of blood cause a more intense blue, but almost always a turbid or opaque blue, often the color of a turquoise.

If the reaction is intense it may be better seen if about 10 c.c. of ether is added to the original extract. If smaller amounts of blood are present

<sup>1</sup> American Journal of the Medical Sciences, March, 1907, p. 408.

the reaction may assume a smoky, grass-green color. (See later.) The reaction may be sometimes intensified by extracting the greater part of the coloring matter with alcohol, which may be filtered off. This makes the test long, and it is seldom necessary.

Cowie's observations as to the delicacy of the test are interesting:

1. The guaiac reaction in all of its modifications is constantly markedly more sensitive than the Klunge aloin reaction. There are times when the aloin reaction seems as sensitive as the guaiac.

2. The limit of sensitiveness of the original Boas turpentine method is 0.004 gram of blood per gram of feces. Under certain circumstances it may recognize 0.001 gram of blood per gram of stool.

3. The limit of sensitiveness of the Boas test when dilute hydrogen peroxide is used is 0.003 gram of blood per gram of stool.

4. The limit of sensitiveness of the author's water and turpentine modification is 0.00035 gram of blood per gram of feces.

5. A color that appears and gradually fades is the crucial test of a positive guaiac reaction.

6. The limit of sensitiveness of the Klunge aloin test is 0.02 gram of blood in 1 gram of feces. Under certain conditions a questionable or very faint reaction occurs with 0.015 and 0.004 gram, respectively.

His observations upon the effect of the ingestion of blood are of more clinical importance:

1. In order that a positive reaction for occult blood occur in the stools after a hemorrhage from the esophagus or the stomach the hemorrhage must amount to 0.5 gram. With such a hemorrhage only a very faint reaction is present. With a gram of blood a decided reaction is always present.

2. The reaction always occurred in the first stool passed after the blood ingestion. The earliest reaction was obtained fifteen and three-quarter hours after ingestion.

3. The reaction was never present in the second stool passed after ingestion.

4. In this series the water-guaiac-turpentine method was much more sensitive than any of the other modifications. Next in point of sensitiveness was the guaiac and dilute hydrogen peroxide method. The aloin reaction did not take place in any case.

His investigations upon the influence of meat diet are entirely negative—that is, he never found a positive reaction after the ingestion of meat. His experience is very different from most, and, I believe, all other observers. I am positive that the ingestion of rare meats, and especially pressed beef juice, will give a very prompt reaction for blood in the stool by the guaiac and aloin tests.<sup>1</sup>

Goldmann<sup>2</sup> says that he has several times found hemorrhoids situated

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1905.

<sup>2</sup> Zentralblatt f. Chir., 1906, xxxiii, Nr. 26.

high in the rectum, 10, 16, or 19 cm. above the anus, which were the cause of hemorrhage from the bowel, of which the cause had not been discovered.

**GASTROTAXIS OR OOOZING OF BLOOD FROM THE MUCOUS MEMBRANE OF THE STOMACH.** It has long been known that free hemorrhage from the stomach may occur without demonstrable organic lesions.

W. Hale White<sup>1</sup> has collected 29 authenticated instances of this condition, including 2 of his own and 5 from the records of Guy's Hospital. He has included only those cases in which an autopsy or operation has confirmed the diagnosis; 27 of these were women and 2 men; 23 patients were in the third and fourth decades. The youngest was a boy of eighteen years.

The disease seldom results fatally and is more common in hospitals than in private practice. The principal symptoms are vomiting of blood and pain in the stomach. The bleeding is often so severe that operation seems the last resort. The attacks of bleeding may occur intermittently over periods of many years, with intervals of freedom from hemorrhage. Pain in the stomach and vomiting without blood usually occur in these cases in the periods of hemorrhage and between them.

The etiology of the condition is obscure. It appears to have nothing to do with vicarious menstruation, as is suggested by the fact that it occurs in men as well as women. Chlorosis does not seem to be a factor, nor was hysteria of frequent occurrence in White's cases. It does not appear probable that the bleeding comes from erosions or in the early stages of ulcer, since the disease may persist for years without the formation of an ulcer. The ecchymoses which are often found in the gastric mucous membrane at autopsy did not seem to be a cause of the hemorrhage in White's cases.

In the absence of demonstrable lesion, or other satisfactory explanation of the bleeding, White assumes that the condition is akin to purpura. The prognosis is good. The diagnosis is often extremely difficult to make, especially from ulcer, although in the latter condition the patient seems sicker and nutrition is interfered with to a greater extent. A high acidity, of course, would favor ulcer. Operation in these cases is entirely unwarranted, for, as would be supposed, gastro-enterostomy has not the slightest effect upon the bleeding. The medical treatment consists of rest in bed, and a proper and nourishing diet. Ergotin is bad, for it raises the general blood pressure. Chloride of iron sometimes is of benefit. Calcium chloride also occasionally seems to have some effect in stopping the bleeding.

**Gastric Ulcer.** **THE PATHOGENESIS OF GASTRIC ULCER.** During the past year the results of three series of experimental observations upon the etiology of gastric ulcer have been published. Together they con-

<sup>1</sup> Lancet, November 3, 1906.

stitute a great step in advance toward a clear understanding of the etiology of the so-called peptic ulcer of the stomach and duodenum.

I need not remind the readers of *PROGRESSIVE MEDICINE* of the numerous attempts to solve the question of the causation of peptic ulcer experimentally and of their failure or only partial success. The means employed to produce experimental ulcers have included mechanical and chemical irritation and injury, including excessive amounts of HCl, general anemia, disturbance of the local circulation and local anemia, and injuries to the nerves and nerve centres.

While ulcers have been produced in many of the experiments, the results have not been conclusive because (1) the ulcers were not typical and did not resemble human gastric ulcer, healing too quickly, and for other reasons; (2) they were not produced with enough regularity to make it probable that the condition causing the ulceration was an important and necessary factor in the etiology of such ulcers.

The three observations that promise to help us toward a satisfactory understanding of this important subject are, first, those of Turck,<sup>1</sup> who found that he could produce gastric ulcers in dogs practically at will by feeding them with cultures of *Bacillus coli* for a varying length of time.

The percentage of positive results in Turck's experiments was practically 100—that is, as I say, he can produce gastric ulcers at will. This indicates that he has discovered a very important if not the necessary factor in the etiology of the condition.

The steps in the formation of the ulcer seems to be a mucoid degeneration of the mucous membrane, and then there forms a necrotic mass whose base is often in the muscularis.

One of the most striking and peculiar of the histological changes noted by Turck was the excessive proliferation of the acid or parietal cells about the edges of the necrotic area. This change, as far as I know, has never been noted in the human subject.

The exact mode of formation of the ulcer has not been worked out, but if Turck's work is confirmed it is a great addition to our knowledge of gastric ulcer.

An interesting point in Turck's paper is that he shows, by the examination of 189 healthy or fairly healthy dogs, that gastric ulcer, if not unknown in dogs, must be extremely rare, for no case occurred in the series examined.

Rosenau and Anderson, of the Hygienic Laboratory in Washington, while studying the guinea-pigs used to standardize diphtheria antitoxin, found that in one-half of the animals dying before the tenth day after the injection of diphtheria toxin there were areas of congestive hemorrhage or ulceration near or at the pylorus. This is striking when considered in connection with the fact that all of the animals in which Turck produced

<sup>1</sup> Journal of the American Medical Association, June 9, 1906.



ulcers by feeding with the *Bacillus coli* showed signs of a severe toxemia, such as hemolysis and necrosis of the liver, kidney, and stomach, and yet there was no evidence of bacteriemia or any local focus of suppuration.

It suggests that perhaps toxemia is the important element, and not infection by the microorganisms themselves.

Fütterer's<sup>1</sup> experiments approached the subject from a slightly different standpoint. He excised a small piece of mucous membrane of the stomach and then kept the animals in a state of chronic anemia by giving them blood-destroying substances. By doing this he kept the ulcer from healing and produced ulcers that very closely resembled the human gastric ulcer. These ulcers were most typical when produced in the pyloric end of the stomach near the lesser curvature. The therapeutic value of these observations are, of course, manifest.

It has already been shown by Turck that close confinement with a scanty supply of air, even if the surroundings are kept sterile, may produce ulcer and certainly predisposes to it.

The work of Turck and of Rosenau and Anderson show that a very important factor in the production of gastric ulcer is intoxication by a toxic substance, probably quite easily by the poison contained in the *Bacillus coli*, but often by the toxin of the diphtheria bacillus as well, and perhaps of other microorganisms also.

The experiments of Fütterer and Turck also show that the process is a complex one, and that the formation of gastric ulcer is not due to any one course or set of courses.

**SOME FACTORS PREVENTING THE CURE OF GASTRIC ULCER.** The cure of a gastric ulcer is accomplished by the observance of rest and the institution of a diet which puts the least possible strain upon the digestive powers and motility of the stomach. According to F. Tecklenburg<sup>2</sup> distention of the stomach is the most important factor which prevents healing of an ulcer. The organ is one whose anatomical structure and relations render it especially liable to distention, and ulcers are with the greatest frequency situated in those parts which are most subject to the distressing influences. The possible causes of distention, met with in practice, may be divided into three groups: (1) Distention by food and drink; (2) muscular atony; (3) nervous conditions (aërophagy and gastrosuccorhea). Where the gastric ulcer has been diagnosticated, the first of these causes may be avoided by feeding in small quantities at frequent intervals. In some cases, however (*e. g.*, in anemic girls), the ulcer may not be recognized and the main indication for overfeeding may be followed to the detriment of the gastric condition.

Muscular atony of the stomach is a factor in the prevention of a cure, when the patient begins to get out of bed and assumes the upright position. It happens that atony occurs frequently in just those cases

<sup>1</sup> Festschrift f. Rindfleisch, 1907, p. 89.

<sup>2</sup> Archiv f. Verdauungskrankheiten, 1906, Band xii, Heft 6, p. 517.

where there is a predisposition to ulcer formation. The insufficient nutrition of the gastric walls, which occurs as a result of general anemia, may form the basis upon which both atony and ulceration may arise. Through the hemorrhages caused by the ulceration a vicious circle may be set up. When the patient is put to bed and a strict cure is instituted, the atony disappears as a factor. But when the ulcer is in a fair way to heal, and the patient is allowed to get out of bed, atonic distention of the stomach may again undo all that has been accomplished.

In order to prevent this complication, the author advocates building up the strength of the patient before the strict treatment of the ulcer is commenced. This is practicable in cases where there is no hemorrhage. The patient should be put to bed and fed in smaller quantities at frequent intervals. Alkaline waters and the administration of atropine will combat the excess of hydrochloric acid. Cream, butter, and eggs are among the most valuable articles of diet. Various local measures for improvement of the gastric atony may be practised, such as epigastric douching or cold sponging, support of the stomach by abdominal binders, gymnastic exercise of the abdominal muscles, electricity, etc. Internal douching may be practised in cases where there have been no hemorrhages for six to eight months. The author has also seen benefit result from the subcutaneous administration of sodium cacodylate. After the atony, which has hitherto prevented the cure of the ulcer, has been removed by these means, a fresh start may then be made in the treatment of the ulcer itself. The diagnosis of atony complicating gastric ulcer is best made by an observance of the periodic occurrence of the gastric disturbances; a period of well-being is suddenly interrupted by the onset of severe symptoms, which gradually disappear, then recur, etc. In such a case the institution of the above-described treatment is the only alternative for surgical intervention. Still, this line of procedure may be impossible in the following cases: (1) Where the patient's social condition prevents the devotion of so much time to the cure; (2) where hemorrhages indicate immediate institution of treatment for the cure of the ulcer; (3) where the above treatment is accompanied by pains and other symptoms, which show that the patient will receive no benefit from it. Cases that have been subjected to this line of treatment without effect must be turned over to the surgeon. The indications are for a gastro-enterostomy, the lower part of the stomach being selected as the site of the anastomosis.

It has been mentioned before that nervous influences constitute a third factor in the prevention of healing of a gastric ulcer.

**THE EFFECT OF AEROPHAGIA UPON GASTRIC ULCER.** Aërophagia may be taken as an example of these nervous phenomena. It occurs in nervous or hysterical individuals. The air may gain access to the stomach by being swallowed with saliva and food, or by aspiration, or by actual swallowing of air. The first method is of frequent occurrence, and cannot be considered pathological. The second possibility, aspiration, would

depend upon the active participation of the stomach in a manner similar to the compression and expansion of a rubber ball; the possibility of this is denied by some authorities.

The most probable explanation of the phenomena is the third possibility, or true *aërophagia*, which is often preceded by an eructation of gas. The condition varies in degree from the mild state of nervous eructation to that state in which large amounts of air accumulate in the stomach—a condition termed “*pneumatosis*.” *Aërophagia* is entirely independent of the state of gastric function, and seems to be purely a nervous condition. The author has found it in catarrhal conditions with subacidity, and also in quite a number of ulcer cases. In the latter the *aërophagia* may depend (1) upon a purely neurotic basis, (2) upon pain, and (3) upon the element of fear, *e. g.*, fear of a repetition of hemorrhage. The baneful influence of *aërophagia* upon gastric ulcer lies in the consequent distention of the stomach. What was said concerning muscular atony also applies here, except that the disturbance is greater than in the former condition. There are two reasons for this, namely, (1) that the distention in *aërophagia* is apt to be greater and more variable, and (2) that the stretching occurs in all directions, instead of downward only, as in muscular atony. In treating such cases the patient should be instructed as to the nature of the condition, and should be advised to inhibit voluntarily the acts of eructation and swallowing. He may be greatly assisted in his endeavors by keeping the mouth open, by either natural or artificial means. Attempts should also be made to improve the nervous tone of the patient. When the ulcer persists in recurring in spite of all treatment, gastro-enterostomy is indicated.

Theoretically, *gastrosuccorhea* may complicate gastric ulcer and prevent its cure by distention, but no such case has ever been recorded.

**MORBID PHYSIOLOGY OF GASTRO-ENTEROSTOMY.** The operation of gastro-enterostomy is one of the surgical procedures which lie particularly upon the borderland of medicine and surgery. The effect of the operation upon the physiology of digestion is more important for the physician than for the surgeon, because the latter (fortunately for him) has usually nothing to do with the remote after-treatment of such cases. We find that the results of the operation are quite complicated and also quite different from what we supposed.

Three papers have recently appeared which deal with the subject very thoroughly and scientifically. They are by Cannon and Blake,<sup>1</sup> Katzenstein<sup>2</sup>, and by Herbert Paterson.<sup>3</sup>

Both Paterson and Katzenstein state that there is regular regurgitation of bile and pancreatic secretion into the stomach after the opera-

<sup>1</sup> *Annals of Surgery*, May, 1905.

<sup>2</sup> *Deutsche med. Woch.*, January 17, 1907.

<sup>3</sup> *Hunterian Lectures*, London, 1906; *Journal of the American Medical Association*, August 24, 1907.

tion. Both observers agree that this does not interfere decidedly with gastric digestion. Paterson did his experiments upon human beings, and concludes that the regurgitation of bile and pancreatic juice is very slight, usually so little that it can rarely be detected by Gmelin's test, and so must be under 5 per cent. Hence, in Paterson's opinion the amount of intestinal contents is too small to interfere with gastric secretion. Katzenstein, basing his observations upon experiments upon animals, believes that considerable bile and pancreatic juice regurgitates, but it does not affect either peptic or pancreatic digestion, because he finds that the pancreatic ferments do not become inactive in a slightly acid medium. Of the two theories, it strikes me that Paterson's is the most probable, unless Katzenstein can substantiate his statements concerning pancreatic digestion.

All observers agree that the acidity of gastric secretion is lowered after the operation. That this is not due to chemical neutralization with bile or pancreatic juice is shown by the fact that the chlorides are not diminished. Neither Paterson nor Katzenstein give clear or satisfactory explanations for this decrease in acidity. It seems to me that it may be due to the inhibitory action that bile is known to exert upon gastric secretion, which is reflex, of course, and not chemical neutralization.

Whatever the reason is, it seems settled that gastric acidity is lowered, and this may be the explanation why the operation of gastro-enterostomy helps the healing of gastric ulcers, even when there is no pyloric stenosis and, consequently, when there is no question of drainage.

This brings us to another very interesting point, namely, that apparently the operation has no effect upon the gastric motility, provided that there has been no pyloric stenosis before operation. This has been established by Cannon and his associates,<sup>1</sup> who have shown that the gastric contents by preference leave the stomach by the natural paths, even in the presence of an artificial opening.

Cannon gives this summary of his results: He does not consider gastro-enterostomy a drainage operation. In the stomach there are peristaltic waves going toward the pylorus. There results from these waves increased pressure on the food as the pylorus is approached. If there are two openings for the food to go through, namely, the pyloric opening and the stoma, the food will go through the pylorus rather than through the stoma. Another result of these waves is that the peristalsis, as it mixes the food, mixes it in the pyloric end rather than in the cardiac end of the stomach. The food comes out through the pylorus as a thin fluid. It does not go out through the stoma because of the thicker consistence the food has in regions somewhat remote from the pyloric opening. The observations which Blake and Cannon made were made with the Röntgen

<sup>1</sup> *Annals of Surgery*, May, 1905; *Journal of the American Medical Association*, 1907, August 24, Discussion.

rays, and there has been some question whether the pictures seen were true pictures. However, their results have been recently confirmed by observations made in the College of Physicians and Surgeons of New York City. A string was fed to dogs with a small bag of shot tied to the end of the string. In almost all of the cases it was found that the string passed out through the pylorus and thus into the small intestine. Many other observations were also made. The stomach was connected with the lower ileum and also with the colon, and the animal, for a time, gained in weight, which could not be possible if the food did not go out through the pylorus. Cannon thinks we are justified in concluding, therefore, that when there is a double way, the natural and artificial, the natural passage will be taken and not the artificial. Paterson, he said, mentioned one case in which they had a large opening, and stated that the food went out both ways. That was true only when fluid food was given; in this case semisolid food went out only through the pyloric opening and through the stoma. Paterson has confirmed these observations of Cannon in the human being.

The objection which has been advanced, that the acid-pancreatic reflex from the duodenum, which depends upon the formation of the hormone secretin, is disturbed in gastro-enterostomy, is set aside (1) by the work of Werthheimer, who has shown that free HCl in the jejunum will stimulate the pancreas by the production of secretin as well as in the duodenum, and (2) by the observations of Cannon, which show that the pylorus is still the path of preference for the gastric contents after a gastro-enterostomy.

Lastly, all observers agree that metabolism is not disturbed by gastro-enterostomy, as shown by the absorption of N, fats, and carbohydrates.

**Peptic Ulcer of the Esophagus.** Peptic ulcer of the esophagus was first described by Albers in 1839. Since then the subject has received attention from Rokitsansky, Flower, Reeves, Quincke, Chiari, and others. The fact seems to be fairly well established that peptic ulcers similar to the ordinary gastric ulcer may occur in the esophagus. The condition has received but little attention in this country, although not exceedingly rare, and the thorough consideration of the subject by Tileston<sup>1</sup> is very timely.

A study of the Records of the Massachusetts General, Boston City, and Long Island Hospitals shows that peptic ulcers were noted in 6 cases in 4496 autopsies, or 0.13 per cent. It is, therefore, not a common condition, but we should remember that gastric ulcer itself is not very frequent. It occurs from infancy to old age, but is not common in the fifth and sixth decades. In 40 cases collected by Tileston, 28 were male and 12 female. In order that peptic ulcer should be formed it is evidently necessary that the cardia should be insufficient, allowing the regurgitation of gastric

<sup>1</sup> American Journal of the Medical Sciences, August, 1906, p. 240.

juice into the esophagus. Frequent vomiting should, therefore, play an important part in the causation and diseases such as nephritis, peritonitis, chronic gastritis, and especially gastric and duodenal ulcer should favor its occurrence. This is found to be the case.

Stenosis of the pylorus was present in 23 per cent. of the cases. Alcoholism, arterial sclerosis, and trauma are also predisposing causes. The gastric secretion was examined in 7 cases, but the results were not accurately recorded and no deductions can be drawn from them. Large abdominal tumors were present in 3 cases. Quinke suggests that upward pressure of such masses may cause kinking of the esophagus and favor the development of esophageal ulcers.

Guitéras has described a case in which nervous spasm of the esophagus appeared to have favored the ulceration. Chronic interstitial nephritis was noted in 4 cases, in 1 of these combined with amyloid liver and spleen. Tuberculous peritonitis and acute general peritonitis were each present twice; the latter was due to perforation of a gastric ulcer and of the gall-bladder, respectively. Cirrhosis of the liver and phthisis were each present in 2 cases. In the case of Dasse there was an aneurysm of the aorta, the size of a hen's egg, adherent to the esophagus. The aneurysm was situated at the fourth dorsal vertebra, the ulcer 4 cm. above the cardia; the distance between the two renders any direct causal relationship doubtful.

Simple ulcer of the esophagus resembles very closely, both in gross and microscopic appearances, simple ulcer of the stomach. It is situated, as a rule, in the lowest part, close to the cardia, as one would expect from the peptic origin. Usually it stops short at the cardia; in 6 cases however, or 17 per cent. of the 36 cases which came to autopsy, it involved the adjacent part of the stomach also, and the appearance of the ulcer pointed to a primary seat in the cardia, with the invasion of the esophagus by direct extension. The size varies greatly, from that of a pea or smaller to ulcers involving the entire surface from the cardia to the bifurcation. In most of the cases (81 per cent.) but a single ulcer is present; in others they are very numerous.

The ulcer, like its namesake in the stomach, has a strong tendency to perforation, which took place in 6 cases: twice into the right pleural cavity, once into both pleural cavities with double pneumothorax, and once each into the aorta, pericardium, and lesser omental cavity. In Janeway's case, without actual perforation, there was inflammation of the periesophageal tissue, pericarditis, and pleurisy.

Healing takes place frequently, with the production of a scar. Scars were found, either alone or in conjunction with fresh ulcers, in 9 cases, or 25 per cent. They may be puckered and radiating, as in the stomach. If small, they do no harm; the larger ones by contraction produce stenosis. In 1 case (Ortmann) a carcinoma of the esophagus was found developing from the scar of an old peptic ulcer; Tileston has

seen the specimen from a similar case at the Pathological Institute in Vienna.

In a large proportion of the cases the ulcer was not suspected during life, being entirely latent, or giving rise to no symptoms sufficiently characteristic for a diagnosis. In another group it remained latent up to the time of perforation. The symptoms vary in different stages of the disease according as the ulcer is opened or healed. The most prominent manifestations of the stage of ulceration are five, namely, pain, dysphagia, vomiting, hematemesis, and perforation. The characteristic location is at the xiphoid cartilage, or beneath the sternum, radiating to the back between the shoulder-blades. In some cases it was referred by the patient directly to the lower end of the esophagus, in others to the front of the chest. In a few instances the pain was epigastric, although the ulcer was situated in the esophagus only. Tenderness to pressure has been observed in the epigastrium and over the lower sternum: No mention is made of tender points in the back analogous to those frequently found in gastric ulcer.

The relation to food is important. As a rule, the pain occurs either during the last part of the act of swallowing or immediately afterward, in contrast to the later onset of pain in gastric ulcer. It varies from a slight burning sensation to a pain so severe as to prevent the patient from eating, and to require morphine. It is usually paroxysmal, with intervals of partial or complete relief. The passage of bougies may cause great pain. Dysphagia occurred in about half of the cases and is apparently produced by spasm. Vomiting when present is usually due to some accompanying and complication condition of the stomach. Hemorrhage occurred in about half of Tileston's series. It occasionally may be severe.

Perforation was noted in 6 cases, or 14 per cent. It is generally fatal. Perforations into the pleural cavity is marked by sudden intense thoracic pain, dyspnea and collapse, with signs of pneumo- or hydrothorax. The symptoms differ from those of the so-called spontaneous rupture of the esophagus, in that subcutaneous emphysema is absent. Perforation below the diaphragm gives rise to circumscribed peritonitis of the lesser peritoneal cavity. The onset is usually gradual, beginning with pain and dysphagia; frequently dyspepsia or the symptoms of gastric ulcer precede. In other cases the ulcer remains latent up to the occurrence of hemorrhage or perforation. The course is often remittent and periods of comparative health intervene. Naturally esophageal stricture is of frequent occurrence in the later stages of the disease. The duration in Tileston's list was from a few days up to twelve years. In one-half (63 per cent.) it was under six months. Death took place most frequently from perforation or hemorrhage.

**DIAGNOSIS.** The diagnosis of peptic ulcer of the esophagus is difficult, and in many cases impossible; in others it may be made with a consider-

able degree of certainty. Esophageal ulcer should be suspected in all cases with symptoms pointing to ulceration in the lower part of the esophagus. The diagnosis is practically certain, if other causes of ulceration can be excluded and there are dysphagia, pain during or soon after deglutition, situated under the sternum or between the shoulder-blades, hematemesis or melena, and obstruction in the lower part of the esophagus. Symptoms of present or past ulcer of the stomach or duodenum are very strong confirmatory evidence. Tenderness over the lower part of the sternum, and perhaps also behind, near the ninth dorsal vertebra, should be looked for.

**PROGNOSIS.** Peptic ulcer of the esophagus is a serious affection, not only from the danger of hemorrhage and perforation, but also owing to the marked tendency to the formation of stricture, which, though often yielding readily to dilatation, is very likely to recur. Furthermore, it is often a complication of grave diseases, which of themselves bear a bad prognosis. The number of cases diagnosticated during life is yet too small to justify any conclusions as to the exact mortality.

**TREATMENT.** The indications for treatment in the stage of ulceration are the same as for gastric ulcer. In order to provide conditions favorable for healing, irritation of the ulcer by the passage of food should be reduced to a minimum. Hence, rectal feeding will be in part for a short period, with rest in bed, to be followed by a Leube cure. All articles of diet which might cause mechanical, thermic, or chemical irritation are to be avoided. The general condition of the patient should receive careful attention.

Among drugs which, when given by the mouth, may have a direct action on the ulcer, silver nitrate ( $\frac{1}{4}$  to  $\frac{1}{2}$  grain, well diluted, three times daily) and bismuth subnitrate (15 grains in suspension once daily) should be mentioned. It is probable that in some cases the drug will remain in contact with the ulcer long enough to exert a beneficial effect. Direct applications to the ulcer by means of the esophagoscope probably will not be practicable on account of the danger of hemorrhage. Lavage of the esophagus is also contra-indicated for the same reason.

**Enteroptosis and Cardiopptosis with Return to Normal.** The etiology of enteroptosis and cardiopptosis has not yet been definitely determined. Many authors ascribe the conditions to congenital defects. In the largest number of cases, however, deficient nutrition seems to be the most important factor. The indication for treatment in such cases is evident. M. Einhorn<sup>1</sup> describes several cases of enteroptosis, nephropptosis, gastropptosis and cardiopptosis, in which a return of the displaced organs to their normal positions was effected by producing an improvement in the general nutritive conditions, with an increase in weight. An explanation of these cures is not readily made, but the improvement seems to be

<sup>1</sup> Berl. klin. Woch., 1906, xliii, Nr 34, 1128.



connected to a certain extent with a deposition of fat around the affected organs, such as the kidneys and heart. Cases of cardiophtosis are among those most readily cured by this means. An increase in the body weight can almost always be accomplished by a systematic increase in the diet. Although a return of the displaced viscera to the normal cannot be accomplished in every case, still the prognosis is almost always favorable.

**A New Reaction for Free Hydrochloric Acid in the Gastric Contents.** F. Simon<sup>1</sup> gives a delicate test for free hydrochloric acid. A pinch of pure, dried, pulverized resin of guaiac is dissolved in 5 c.c. of the following mixture:

Spiritus ætheris nitrosi . . . . .	10
Alcoholis . . . . .	40

The solution of guaiac must be freshly prepared for each series of experiments; 5 c.c. of filtered gastric contents are placed in a warmed test tube, and the guaiac solution is superimposed. At the point of contact of the two layers the precipitated guaiac forms a grayish-white ring, which is soon colored blue in the presence of free hydrochloric acid. If there is only a trace of acid, the color is green. Lactic acid in solution of 1.25 per cent. or over will also produce a positive reaction, but this high concentration is never obtained in the stomach. A coloration of the ring may, therefore, be taken as a positive indication of the presence of free hydrochloric acid. This reaction is even more delicate than Günzburg's test.

**Alimentary Hypersecretion.** This condition was fully considered in the abstract of Riegel's classical paper in *PROGRESSIVE MEDICINE*, December, 1904. During the past year papers have appeared by Boas,<sup>2</sup> Strauss,<sup>3</sup> and Zweig.<sup>4</sup> In view of the renewed interest in the condition, a review of their papers is not out of place.

The pathognomonic feature of alimentary or digestive hypersecretion, as it is also called, is that the stomach is found almost empty in the fasting condition. The hypersecretion is to be regarded as a secretion neurosis of excitative character, and the quantity alone, and not the quality, of the gastric juice is affected.

Strauss has described a larvated hyperacidity in which there is an abnormal increase in the gastric acidity immediately after a meal. This excess is soon neutralized by a transudation from the bloodvessels, so that a normal acidity may be found one hour after the meal. The characteristics of this condition are (1) the formation of amidulin through the disturbance in starch digestion, (2) an increase in the stomach contents,

<sup>1</sup> Berl. klin. Woch., 1906, xliii, Nr. 44, 1431.

<sup>2</sup> Deutsch. med. Woch., 1907, xxxiii, Nr. 4.

<sup>3</sup> Ibidem, Nr. 15.

<sup>4</sup> Archiv f. Verdauungskrankheiten, 1907, xiii; Heft 2, p. 143.

(3) low specific gravity, and (4) lowering of the freezing point. The increase in the gastric contents is due to the irritation of the undigested starches. Now, in alimentary hypersecretion there is no increase in the degree of acidity; hence, starch digestion is not interrupted. The condition is merely one of increase in the amount of secretion, due to an abnormal excitability of the gastric glands.

The subjective symptoms of alimentary hypersecretion present the variability characteristic of nervous dyspepsia. Nausea and vomiting are rare. There is usually a feeling of fullness and pressure in the stomach, sometimes amounting to more or less pain. Appetite is variable, acid eructations are common, pyrosis rare. General nervous symptoms frequently coexist with the local manifestations. The most prominent symptom is a rapid loss of weight, due principally to voluntary limitations in diet. Constipation is frequent. There is usually evidence of a congenital predisposition to disturbances of the digestive nervous system, characterized by general weakness of the muscular and skeletal apparatus, an acute costal angle, floating tenth rib, enteroptosis, and more or less disturbance of nutrition. Gastric splashing sounds can usually be obtained, but cannot be regarded as at all characteristic of this condition. They can be obtained in any condition where there is gastroptosis with considerable extent of contact between the stomach and the anterior abdominal wall.

The diagnosis of alimentary hypersecretion rests upon the demonstration of an excess of secretion in the gastric contents. This may be accomplished by a consideration of the ratio between the solid and fluid constituents of the centrifugated gastric contents, expressed from the stomach one hour after a test breakfast. In normal conditions the solid parts form 40 to 60 per cent. of the whole, while in alimentary hypersecretion this percentage is always under 30. In cases complicated by atony the absolute amount of the solid residue will be above the normal, which has been found to be 77 c.c. Tested in this way, atony has been found to be an uncommon complication of alimentary hypersecretion.

The degree of acidity is varying in this condition. The specific gravity of the gastric contents is always below normal—1007 to 1012. The degree of starch digestion depends upon the acidity. In 2 cases a transition from the alimentary into the continuous form of hypersecretion could be demonstrated. The course of alimentary hypersecretion is always chronic and of long duration.

The treatment corresponds closely to that of nervous dyspepsia. Regulation of the diet is important. There should not be more than three meals a day. Proteids and fats are preferred to carbohydrates. Among the proteid foods, eggs, milk, fish, etc., are less irritating than meats. Fats are of great value in diminishing gastric secretion, and also in increasing the patient's weight. Only the easily digested carbohydrates should be given. It is not necessary to limit the amount of bever-

ages. All acids, spices, aromatics, etc., must be avoided. Alkalies and belladonna derivatives are the most useful drugs in combating this condition. Hydrotherapy, massage, and faradization are of value. Lavage has been found useless.

### THE INTESTINES.

**Chronic Auto-intoxication of Intestinal Origin.** Probably no subject in medicine is surrounded by more false hypotheses than is chronic intoxication of intestinal origin. This is unfortunate because chronic intestinal auto-intoxication is really an important condition, and one that needs much further investigation. Much of the confusion that exists in the minds of the profession concerning its symptomatology, and even the existence of such a morbid state as poisoning from intestinal toxins, has arisen because chronic intestinal auto-intoxication has been made to shoulder the responsibility for very many obscure affections of which the causal factors were uncertain. Too often there was no scientific basis for such an assumption, and, in consequence, gradually chronic intestinal auto-intoxication has come to occupy as discredited a place as has the so-called uric acid diathesis. There is a general tendency at present to regard both conditions decidedly askance.

As I have said, this is unfortunate because intestinal auto-intoxication is really a very important condition, and when we come to properly understand its natural history we may find it occupying a place in internal medicine somewhat akin to arterial sclerosis—that is, it may have much to do with the preservation or impairment of bodily vigor and the premature advance of age.

There is no need for me to point out to the readers of *PROGRESSIVE MEDICINE* how little we really know (1) of the poisons found in the gastro-intestinal tract, (2) of the amount to which they are absorbed, (3) of their toxicity, and (4) of their clinical effect when absorbed. Consequently, it is the height of absurdity to confidently assume that intestinal auto-intoxication is the cause of certain obscure affections which occur in some other part of the body because there is a coincident intestinal disturbance. Yet there is not good ground for the skepticism that such indiscriminate and unscientific use of the term intestinal intoxication produced in the minds of many intelligent observers.

There is no doubt that there is such a condition as chronic poisoning from intestinal products, but its exact character and significance is as yet far from clear. During the past year a very valuable addition has been made to the literature of the subject by the work of C. A. Herter,<sup>1</sup> which is embodied in a recent volume.

It is the best authoritative statement of the subject available at present.

<sup>1</sup> *The Common Bacterial Infections of the Intestinal Tract*, New York, 1907.

**The Functions of the Intestinal Bacteria.** Herter points out that no experimental studies have been really conclusive as to the necessity of bacterial action in the digestive tract for the maintenance of health in adult mammals.

The real significance of the normal intestinal flora probably lies not in any immediate relation to processes of digestion, but in a wholly different direction. It is impossible to avoid the entrance of bacteria into the digestive tract. The obligate bacteria (for example, *B. lactis aërogenes*, *B. coli*, *B. bifidus*) adapt themselves to the secretions of this part of the body and ordinarily hold their own against newcomers. By virtue of their adaptation, they are not ordinarily harmful to their host, but, on the contrary, they are, under some circumstances, capable of doing service by giving rise to conditions that discourage the growth of harmful species which man cannot readily exclude from his digestive tract. I believe that the chief significance of the obligate intestinal bacteria lies in their potential capacity for thus checking the development of other types of organisms capable of doing injury.

**SELF-PROTECTIVE POWER OF THE DIGESTIVE TRACT.** Speaking of the defensive action of the digestive juices, Herter says that the normal human organism is provided with more or less efficient methods of defence against bacterial invaders. The acidity of the gastric juice, for instance, checks the growth of many non-sporulating bacteria and is, in a measure, destructive to most varieties. If, however, bacteria are administered in very large numbers, there is a chance that some of them will find their way into the intestine. This is particularly true when microbes are taken into the empty stomach or into a stomach with defective motility which secretes little gastric juice of low acidity.

Herter then goes on to say: "A long, largely anaërobic intestinal tract, permitting gradual resorption of the contents, is a physiological necessity in order that a loss of water and its detrimental consequences may be spared the organism. The presence in the colon of immense numbers of obligate microorganisms of the *B. coli* type may be an important defence of the organism in the sense that they hinder the development of that putrefactive decomposition which, if prolonged, is so injurious to the organism as a whole. This adaptation is the most rational explanation of the meaning of the myriads of colon bacilli that inhabit the large intestine." This view is not inconsistent with the conception that under some conditions the colon bacilli multiply to such an extent as to prove harmful through the part they play in promoting fermentation and putrefaction. An alkaline reaction of the medium appears to favor their putrefactive functions if peptones be present.

The influence of reaction on the growth of intestinal anaërobes has been studied very carefully by A. J. Wakeman, who found that the growth of putrefactive anaërobes is favored by neutral reaction and restrained by the presence of acids. This explains the favorable influence of milk

(containing lactic acid formers) in controlling putrefactive decomposition in the digestive tract.

**INTESTINAL BACTERIA NOT NECESSARILY HARMFUL.** As I have already shown, the normal intestine contains an amount of bacteria that seems astonishing to one who has not followed the subject closely. These bacteria apparently do not give rise to symptoms. Herter says: "It is likely that in all these cases the pathogenic organisms in question are held in check by other bacteria present in the digestive tract or by the bacteria and the intestinal secretions, so that they are unable to multiply in a significant manner or to gain entry into the cells of the mucous membranes. It seems not unreasonable to suppose that this restraint may be overcome by errors in diet, depressed general conditions, or by alterations in the secretions of the digestive tract, and that thus definite infection by the hemiparasitic bacteria that are present becomes possible.

The considerations just mentioned as applying to these bacteria probably hold equally true of the more saprophytic forms concerned in intestinal putrefaction.

"A variety of conditions may be presumed so to favor the development of these anaërobes that their products, instead of being formed in such small amounts as to be harmless, begin to exert a detrimental effect on the organism. Especially important are influences which alter the character of the secretions in the large intestines or bring there unusually large quantities of partly digested proteid food. In certain conditions of the digestive tract an excessive or even a moderate meal of proteid food will precipitate an intoxication or a seizure of vomiting or diarrhea. There are cases classed as ptomain poisoning in which the digestive tract rather than the food is responsible for the observed disorders."

**INTESTINAL BACTERIA AT BIRTH AND IN EARLY LIFE.** While the intestinal tract begins to harbor bacteria at a very early period of extra-uterine life, still in infancy and childhood the numbers of bacteria are smaller and the products of putrefaction are less in amount than in adults.

**INTESTINAL BACTERIA AFTER CHILDHOOD.** Toward adult life great differences exist in the habits of different persons, and these are in a degree reflected in the nature of the bacterial processes of the digestive tract. In adult life the individual experiences new responsibilities, new dangers, an enhanced emotional life, and often a larger proportion of indoor life and more sedentary habits. The dietary is apt to undergo an alteration in the direction of increased and frequently injudicious liberty and the use of tea and coffee. Also the use of tobacco and alcoholic drinks is either increased or begun. Sooner or later these things lead to slight derangements of digestion which manifest themselves clinically. One occasionally meets with persons of unusually robust physical and mental health in whom the bacterial conditions of adolescence persist

until the fiftieth year, or longer. A large proportion of persons, however, by the time they reach the age of fifty, present different physical conditions, although they are in no sense in a state of invalidism, but work hard and most of the time feel well. While in such persons the fecal flora shows nothing striking, it is usually not difficult to demonstrate that the number of putrefactive anaërobes in the intestine is larger than in healthy adolescents. In short, we find in middle life a large number of persons whose health is good or fair, in whom the putrefactive processes are distinctly more active than is the case with most younger persons of normal health.

These persons, though in good health, are not robust. A period of sustained hard work is followed by considerable mental and physical fatigue. Dining out and the use of alcoholic drinks are indulgences quickly followed by unpleasant consequences. Exercise out-of-doors becomes more and more a necessity. The individual is conscious that it requires careful living to keep him in a condition compatible with the performance of his duties.

The main difference between the putrefactive conditions found at fifty and seventy is that at the latter period they are a little more marked in their intensity and affect a much larger proportion of the population. The subjects in question at this later period of life are not ill, but in order to keep fairly well have to be very careful as to their habits of living. They are moderately anemic and easily develop slight disorders of digestion. They weigh less than formerly, and, though they may still be well nourished in appearance, are conscious of losing strength from year to year. They are undergoing what is usually regarded as normal involution. It may be confidently asserted that the onset of senility may be distinctly accelerated through the development of intestinal infection in which the putrefactive anaërobes are prominently represented. I have observed this in cases where it has appeared certain that other toxic causes of premature senility could be excluded.

**The Chemical Products of Intestinal Fermentation and Putrefaction and their Pathological Physiology.** By fermentation is meant the decomposition of carbohydrates and fatty substances, and putrefaction means the cleavages of proteid and allied substances. These two processes furnish some products in common, such as  $\text{CO}_2$ , and some volatile fatty acids, and, furthermore, they are closely associated in that excessive fermentation in the digestive tract almost always leads to excessive putrefaction as well.

**PUTREFACTION IN THE INTESTINES.** Putrefactive changes as opposed to fermentative are produced largely by anaërobic bacteria. In the mouth the caries of the teeth appear to be due to the action of anaërobes whose growth is possible in the masses of food that lodge between the teeth. The use of the tooth-brush not only removes the culture medium, but allows free access of oxygen, and this doubly hinders the anaërobic

growth. In the stomach anaërobic growth is favored by stagnation and insufficient HCl secretion.

The reducing action of raw or rare meat probably favors the development of anaërobic conditions, and certain forms of excessive intestinal putrefaction in man are helped by excessive meat eating.

It is possible that a mild degree of acidosis may be produced for fermentative processes.

The main difficulty in demonstrating the existence of a general toxemia from absorption of poisons from the digestive tract has been that the substances which have been isolated from the intestinal contents are none of them very toxic in animal experiments. Furthermore, we know very little of the method of the formation of even these known substances. Still, the clinical evidence in favor of the existence of a chronic intestinal auto-intoxication is so strong that we are forced to assume that either substances are formed and absorbed which are really toxic, or that our ideas of toxicity derived from animal experiments are misleading.

Herter considers the various substances that have been isolated and studied as follows:

*Basic Substances.* Although ammonia is regularly formed in the course of putrefaction in the intestines, it is probably present in too small quantities to be toxic. The organism is well adapted to care for moderate quantities of ammonia which, as is well known, is united with carbon dioxide in the liver and elsewhere to form urea.

*Putrescin and Cadaverin.* Although the study of the conditions under which putrescin and cadaverin are formed in the intestinal tract is of much biological interest, there is at present little evidence that theses diamines are ever formed in sufficient quantities in the human intestine to constitute in themselves factors in the production of states of intoxication. The association with cystinuria is a striking fact, and the further investigation of this condition will doubtless give us the explanation of the relationship between the production of diamines and the formation of cystin, if, indeed, there be any necessary relation.

*Sulphur Compounds.* The sulphur compounds resulting from putrefactive decomposition in the intestines have received little attention from the standpoint of their pharmacological action. It is very difficult at present to form a just estimate of their importance in intestinal intoxications.

There is reason for thinking that the production of hydrogen sulphide in the digestive tract is of more importance to the organism than the formation of mercaptan. This gas is regularly formed in the intestines, and its presence can be demonstrated in freshly voided feces. The mixed fecal flora, both in health and disease, produce hydrogen sulphide in cultures containing partially hydrolyzed proteids (bouillon). In health probably hydrogen sulphide is formed only in the colon and perhaps in the lower part of the ileum. There are, however, pathological conditions in

which it occurs in the stomach. It is not necessary to assume the presence of a pathological organism in these cases, as it is well known that *B. lactis aërogenes* and colon bacilli liberate it when growing in certain media.

We have at present very little satisfactory knowledge of the influence of hydrogen sulphide on the organism in cases where the gas is liberated in the intestine. Senator and others have described poisoning by this gas. Among the symptoms which have been met with in such cases there have been prominent those pointing to disordered function of the central nervous system, including headache, dizziness, delirium, mental depression, drowsiness, stupor, and collapse. Somewhat similar manifestations have been observed in experimental poisoning by hydrogen sulphide in animals and men.

**AROMATIC PRODUCTS OF PUTREFACTIVE DECOMPOSITION.** *Phenol and Cresol.* In some pathological conditions attended by excessive putrefaction in the intestine these substances are found in the intestinal contents in amounts considerably above the normal, which is always small. But one never, however, finds them in large quantities—never so much, for example, as in the case of indol. Notwithstanding this, the quantity excreted in twenty-four hours in the urine as phenol-potassium sulphate may be fairly high owing to the fact that phenols are produced in the organism in the course of the metabolism of normal cells. In certain putrefactive cases Herter has found these substances in considerably greater amounts in the urine, but even here, however, it does not appear that the phenols can be regarded as important toxic agents, although it is likely that the continued absorption of moderate quantities from the intestine over a long period of time may harm the cells of the liver and other structures concerned with the pairing of phenol and sulphuric acid, especially if the cell protoplasm of the liver has previously been somewhat damaged.

*Skatol.* This substance is formed in very small quantities from time to time in some normal persons, and very abundantly in some persons suffering from excessive intestinal putrefaction. Usually the amount is much less than that of indol, but this rule is not invariable. Like indol, it is derived from tryptophan, but what are the conditions, bacterial and other, that determine its formation rather than the formation of indol, we do not at present know. Herter has found that the administration of skatol to monkeys by the mouth and by subcutaneous injections has been followed by the appearance of a substance in the urine giving the Ehrlich dimethylamidobenzaldehyde reaction, and that the administration of 0.1 gm. of skatol to man has heightened the Ehrlich reaction in the urine. In most cases in which the feces contain considerable skatol the urine gives a strong reaction with Ehrlich aldehyde. Skatol behaves in the organism much like indol as respects its toxic properties, but it is somewhat less poisonous. There is seldom reason to attribute to it any definite



pathological effects. It is possible, however, that, like phenol, it may, under some conditions, play an auxiliary part with other substances in damaging living cells.

*Indol* is not a product of tryptic digestion of proteids and probably cannot be formed in the course of physiological processes without the intervention of organized ferments such as bacteria. The indol produced in the intestine is, like skatol, derived from tryptophan. In early life the production of indol in the intestines is in general very slight and there are some older persons also who, even while suffering from disorders of digestion, do not form indol. On the other hand, the production of considerable quantities of indol in the large intestine is a feature in many instances of intestinal putrefaction and in some cases the quantity formed is large. That indol may be absorbed in considerable amounts is shown by the appearance of large quantities of indican in the urine of persons in whom the intestine contains large amounts of indol.

While it is true that in general the aromatic compounds are resistant to oxidation, it is probable that whenever indol is introduced in moderate quantities into the organism of carnivorous and omnivorous animals, a portion of it is burned completely in the body. It may be regarded as settled that the liver, muscles, intestinal epithelium, and other cells normally exert a protective action to the nervous system in screening it from the effects of an injurious percentage of indol in the blood, by the ability of these structures to quickly bind any indol which comes to them. The differences in the observed toxic effects are probably dependent on inequalities in different persons in their ability to oxidize indol and to pair it with sulphuric acid. As to the effects of absorbed indol on the organism in disease, it is necessary to speak with caution, since there is no evidence that indol is the only toxic substance absorbed in those cases where it enters the organism from the gut.

The idea that the circulation of free indol in the blood may act in a depressing manner on the muscular structures is suggested by the rapid muscular fatigue which comes on in some persons who have suffered for a long period of time from a high grade of indicanuria. In some cases of excessive intestinal putrefaction in childhood associated with retardation in growth and abdominal distention, there is clearly a poisoning of the muscular system. These children show signs of fatigue very rapidly, and in some cases where the condition has come on in early life they are slow in learning to walk. Their urine contains not only a large amount of indican, but a considerable quantity of phenol. It is likely that phenol in these cases plays a part in the muscular depression. Perhaps in some instances it is as much a factor in inducing fatigue as is indol.

INDIVIDUAL SUSCEPTIBILITIES AS POSSIBLE FACTORS IN DETERMINING CLINICAL TYPES. Herter suggests that individual susceptibility and reaction plays an important part in determining the clinical manifestations of intoxications. The different types of poisoning from absorption

of intestinal contents are explained by the individual cellular reaction of the patient rather than by the poison.

Among half a dozen persons suffering from extreme indicanuria one suffers from headache, sometimes migraine-like; another is prone to lumbago; another perhaps has epileptic seizures; another has mental depression; another progressive muscular atrophy, and still another suffers from cyclic vomiting. There is good reason for suspecting that very similar processes in the digestive tract lead in one case mainly to digestive disturbances, and in others, owing to a lesser sensitiveness in the digestive tract itself, to better absorption of poisons and the development of more remote consequences, such as acute arthritis, anemia, or nervous disorders. That the mental and emotional peculiarities of individuals have a large part in fixing the type of nervous reactions that occur in consequence of intoxications has become apparent to careful students of pathological conditions.

**TYPES OF CHRONIC EXCESSIVE INTESTINAL PUTREFACTION.** Herter believes there are three types of the condition:

1. The *indolic type* of chronic excessive intestinal putrefaction. This is marked by striking indicanuria and probably is due to members of the *B. coli* group.

2. The *saccharobutyric type* of chronic excessive intestinal putrefaction, which seems to be initiated chiefly by the anaërobic forms. In its simplest examples there is very little indol in the gut.

3. A *combined type*, or cases combining the characteristics of Groups 1 and 2.

*Indolic Type of Chronic Excessive Intestinal Putrefaction.* In these cases the members of the *B. coli* group form indol in considerable quantities and they probably invade the small intestine in large numbers. The bacterial cleavages seem largely to replace normal tryptic digestion.

Provisionally we may classify here that type of chronic intestinal digestion found in marantic children with large abdomens. In the treatment of these children much patience is necessary. At first their digestive processes must be improved. Carbohydrates should be greatly restricted and should be given as rice or Huntley and Palmer biscuits. The milk may be peptonized to promote its earlier absorption. Chicken, beef, and mutton are permissible, but they should be finely divided. In a child five or six years old it may be advisable to give only two meals a day. Considerable benefit seems to follow daily irrigation of the colon, which facilitates the removal of the putrefactive products before they are absorbed. The children should exercise, but should be spared fatigue. They should rest much. Because they stand cold badly, they do best in a mild climate during the winter. Improvement may be possible after several years of rigid *regime*. The retarded growth, however, is evident even at puberty. Some of these patients seem always susceptible to intestinal disorders, and may never become strikingly robust.

*The Saccharobutyric Type of Chronic Excessive Intestinal Putrefaction.* In this type the seat of the putrefactive process is the large intestine and lower ileum. It is due to the activity of the strictly anaërobic butyric-acid-producing bacteria. Although our study is not yet exhausted it may confidently be stated that in many cases *B. aërogenes capsulatus* is largely responsible. With this form may be associated *B. putrificus* and possibly sometimes the bacillus of malignant edema, although often these forms are not found in cultures on any of the ordinary media.

The abundance of putrefactive anaërobes, especially of *B. aërogenes capsulatus*, gives a peculiar character to the intestinal contents. The organisms attack carbohydrates and proteids vigorously and butyric acid is formed from both, together at times with propionic, caproic, or valeric acid. These acids are largely responsible for the odor of the stools. From proteids, besides these acids, hydrogen, carbon dioxide, and perhaps methane are formed. As a consequence the feces have a low specific gravity and often a decidedly light color. The presence of hydrogen leads to the extensive reduction of bilirubin and other pigments. The Schmidt test with mercury bichloride gives a strong pink color. The stools have an acid reaction, although the acids are neutralized in part by ammonia and other bases formed in the process of putrefaction. It is probable that the ammonium butyrate acts as an irritant to the gut, causing soft stools or diarrhea. Indol is absent or present in small amounts. Phenol occasionally is found in slight excess. In the urine the ethereal sulphates at times are excessive, although the reason for this is not clear. Mercaptan may be present in the feces as a trace: it also is found in cultures by means of the isatin-sulphuric-acid test. It has been noted that as the patient improves the mercaptan becomes less or disappears, but the explanation of this phenomenon is at present unknown.

In nearly all adults the *B. aërogenes capsulatus* is present in the intestines in small numbers. It is possible that this organism is responsible for repeated slight attacks of intestinal putrefaction, although it may not in these mild cases lessen the duration of life. In some persons in whom a high grade of putrefaction is present, a condition of actual invalidism may be induced and life may be definitely shortened as a consequence of the intoxication.

The presence of ammonium butyrate may give rise to irritation of the intestine, and this may be associated with an excessive desquamation of the epithelium, not only in the intestine, but in the mouth and the stomach as well. We have evidence of this in the presence of a large number of nuclei in the feces, and it is well recognized that excessive desquamation of the lingual epithelium is associated with digestive disorders. The patients suffer from flatulence. They tolerate carbohydrates and acids badly, and are very liable to attacks of diarrhea after a meal of carbohydrates. Acids may be formed in the mouths of these patients through the influence of anaërobes. This adds to the irritability of the intestine.

It is possible that in advanced cases the *B. aërogenes capsulatus* may invade the small intestine and there find sugar from which to form butyric acid, etc. After the carbohydrates are thus exhausted, the anaërobic forms in the large intestine set up putrefactive processes in the proteids which exist there.

It is also noteworthy that many patients who suffer from severe intestinal putrefaction are distinctly anemic. The first change in the blood seems to be a decrease in its volume; then the hemoglobin falls somewhat and finally the cells themselves are reduced in number. The grade of anemia varies extremely, from a moderate secondary anemia to the most serious grades approaching the type of pernicious anemia.

*The Combined Indolic and Saccharobutyric Type of Chronic Excessive Intestinal Putrefaction.* Examples of this type of intestinal putrefaction are common. There are many putrefactive anaërobes in the gut, and also a persistent and well-marked indicanuria, which is but slightly influenced by diet. The nervous symptoms are relatively prominent and appear early. They are emotional irritability and periods of mental depression; muscular or mental activity soon induces a striking fatigue. Later the blood disturbances may appear. Although these patients have intervals of improvement that continue for months, on the whole the general tendency is downward. They become less robust and recuperate less promptly from every succeeding attack. They may run along for ten or fifteen years in a weak condition, with periods of slow improvement, and finally may present the picture of a pernicious anemia. In others the nervous symptoms increase and the patients may need treatment in a sanitarium or in an asylum for the victims of melancholia.

These various manifestations in different individuals may be merely a differing reaction to the same poison. Whether the nervous system or the blood shall bear the brunt of the attack is determined by the relative vulnerability of these tissues in that particular individual. It is noticed also that under treatment one group of symptoms may improve quite independently of the other.

There is a more rapid advance of invalidism than is the case of either type 1 or type 2 alone. The atrophy of the fat and muscle and the blood changes are present, and perhaps also there are chronic parenchymatous changes in the kidney and liver as a result of the constant poisonous action.

**THERAPEUTIC CONSIDERATIONS.** The difficulties that beset our efforts to control and modify excessive intestinal putrefaction are obvious. Although the cases arrange themselves in groups, every one presents certain points of difference. Our experience is so incomplete that as yet our efforts are more or less experimental. Notwithstanding this, one may lay down rules for partial guidance that are based on certain principles, but a careful regard for individual traits is imperative.

The mild cases often show a rapid improvement and lose the evidences

of putrefaction. The patient feels well, yet he can hardly be called normal, because he has deficient reserve power and will easily relapse to his former condition after an indiscretion in eating or excessive fatigue or worry. The long-standing cases improve slowly at best. The chemical products of putrefaction may be reduced in amount, but the symptoms often persist, and even under most favorable circumstances the patient is liable to frequent and protracted exacerbations.

The following principles must be regarded in treating all the three types of putrefaction: (1) Avoidance of continued reinfection that follows the ingestion of putrefactive bacteria with the food; (2) the promotion of prompt digestion and rapid absorption from the small intestines; (3) the reduction of the number of putrefactive anaërobes in the ileum and colon.

1. To avoid infection and reinfection the mouth must receive scrupulous care. Carious teeth and gingivitis must be treated carefully by the intelligent use of the tooth-brush and of washes containing peroxide of hydrogen. In conditions of gastric atony a process of putrefaction begins in the stomach that normally starts in the colon. Gastric fermentation and putrefaction are controlled by lavage every day, perhaps best in the morning. The reduction of the number of bacteria here leads to lessened damage to the bowel at lower levels.

In the preparation of food ordinary cleanliness is very effective. It is probably better to use cooked food as much as possible. Fruit is not above suspicion, for Dr. Rettger has determined that the bacillus of malignant edema is commonly present on banana peel. This suggests the advisability of peeling all fruit that is eaten. Milk always contains a large number of bacteria and often some of the putrefactive forms, especially *B. putrificus*. The lactic acid formers abound, but their action is rather beneficial in that they antagonize other and harmful forms. Sterilization of the milk is of little value. Pasteurization or the ordinary boiling kills the lactic acid formers, but does not harm the spores of the putrefactive organisms. Cheese, except fresh home-made cheese, contains many putrefactive forms, and is best avoided, particularly inasmuch as many of these patients lack the protective action of the normal amount of hydrochloric acid in the stomach.

2. With rapid digestion and prompt absorption little pabulum for the putrefactive organisms reaches the colon. These processes are facilitated by measures that improve the secretory and motor functions of the stomach. Chief among these is proper mastication, which largely determines the ability of the body to utilize food. When large masses of meat are swallowed, they commonly appear in the feces. Commintion of food outside the body is not an adequate substitute, for the patient then loses the emotional stimulus to gastric secretion and also the digestive action of the saliva itself. The administration of hydrochloric acid often helps for a time, but in long-standing cases, especially those of the combined indolic and saccharobutyric types, it is of little use. Ferments, such as

pepsin and pancreatin, are of doubtful value, although they cannot be said to be always useless. Diastase gives better results, as it enables the patient to utilize more extensively the carbohydrates of the food. If, as often happens, the stomach is irritable, it is advisable to give small meals and to administer flaxseed or other demulcent before eating. The best pancreatic stimuli, aside from the quality of the chyme, are cheerful emotional accompaniments of eating, and rest, physical, mental, and sexual. Prompt absorption is promoted by restricting the amount of food, especially of proteid food. Meat should rarely be eaten more than once a day.

3. To reduce the number of putrefactive organisms in the colon, one turns naturally to *intestinal antiseptics*. In regard to them, Herter says, while these drugs may act efficiently on bacteria in the stomach, evidence of their continued action in the intestine is variable. Perhaps the salicylates are most likely to check fermentation and putrefaction in the stomach and small intestine. It is conceivable that certain oxidizing substances which are slowly dissociated, such as manganese bioxide, may reach the colon in time to liberate their oxygen there and thus, in part at least, remove the anaërobic conditions that obtain in this part of the intestine.

The use of *laxatives* may be followed by temporary benefit, in that they lessen absorption from the gut, as is shown by a decrease of the ethereal sulphates in the urine, after their use. They must, however, be given with caution, lest they increase the irritability of the bowel and lead to diarrhea and loss of strength. On the whole, they are useful in acute and subacute cases only.

There are certain very tempting methods which aim to substitute harmless bacteria for the putrefactive organisms, but more evidence is needed as to the value of this procedure. It is a common practice to introduce lactic acid formers in Kumyss and Kefir and also in Bacilac, a fermented milk introduced by Metchnikoff, which is free from yeasts. Irrigation of the colon two or three times a week is often followed by a decrease of the ethereal sulphates in the urine and by relief from symptoms, including both the mental symptoms and the anemia. This procedure is more efficacious in the saccharobutyric and combined types of putrefaction.

**PROGNOSIS.** In considering the prognosis of these patients, the duration of the condition is as important as its intensity. Better results are obtained in those cases induced by gross errors of life, the correction of which is followed by improvement or complete recovery. In a highly neurotic person the outlook is less hopeful. A protracted rest for two or three years, with careful attention to the principles of treatment laid down, offers the best hope of health.

**The Connection between HCl Secretion and Putrefaction in the Intestine.** Von. Tabora<sup>1</sup> has attempted to determine the relation that the stomach

<sup>1</sup> Deutsch. Arch. f. klin. Med., 1906, Band lxxxvii, Heft 3, 4, p. 254

secretion bears to the putrefaction processes in the intestines. He did this by employing the Schmidt diet for a period of three days and then a pure milk diet for a like period. This is followed by a period of a diet rich in proteids consisting largely of plasmon and then a fourth period in which the gastric secretion was neutralized by alkalies or suppressed by atropine. He used as an indicator of the intestinal putrefaction the indican and combined sulphates of the urine and the N loss and the indol of the feces. He found that in normal gastric secretion increase of the albumin produced no increase in the products of putrefaction absorbed from the intestine. But when the acid was diminished or absent an increase of albumin in the diet greatly increased the putrefaction. When HCl was given the tolerance of the bowel for large amounts of albumin was greatly increased. In general, even without an increase in the albumin of the diet, von Tabora found a greater amount of indican and indol in low acidities. He concluded, therefore, that the gastric secretion, aside from the direct bactericidal action of the HCl, has a decided influence upon the putrefaction changes in the intestine.

**The Method of Determining the Total Amount of the Fecal Bacteria by Weight.**<sup>1</sup> The most accurate method of estimating the total amount of bacteria in the feces is that devised by Strasburger, which determines the actual dried weight of all the bacteria, whether living or dead.

Attempts to form an idea of the proportion of bacteria in the feces by plating a given quantity and then counting the colonies is inaccurate for several reasons. A large proportion of the intestinal flora die in their passage through the colon and only a relatively small number of microorganisms can be cultivated from the stool. Moreover, the different portions of a stool are far from homogeneous, and what is true of one portion will not be true of another.

It must be remembered that the results obtained by Strasburger's method are entirely quantitative. No distinction is made between the putrefactive and fermentative bacteria, but the whole bulk of the intestinal flora, living and dead, is measured. Which form of bacterial action predominates must be ascertained by other means, chiefly by cultivation, although Ehrlich's aldehyde reaction and the reaction of the feces to litmus may be of some assistance. Through the use of Strasburger's method various facts have been determined concerning the intestinal bacteria, of which many are new and some are at variance with the received ideas of the morbid physiology of the intestines.

1. The *diet* is probably the most important factor in determining the amount of the bacterial growth in the intestines. Foods that are easily digested, and were absorbed comparatively early in their passage through the gastro-intestinal tract, leave little or no residue upon which the bac-

<sup>1</sup> See paper by J. D. Steele, Journal of the American Medical Association, August 24, 1907.

teria can live; consequently, under such a diet, the bacterial count will be low under almost any circumstances. When the diet contains foods which are hard to digest and in which the residue is large, the reverse is the case; consequently, the sort of diet must always be taken into consideration in interpreting the amount of fecal bacteria.

This is easily seen in the following statement, consisting entirely of normal cases: Full home diet gave 18.1 to 20.5 per cent. bacteria; full hospital diet gave 18.2 to 21.1 per cent. bacteria; semiliquid hospital diet gave 15.6 per cent. bacteria; milk diet gave 13.2 per cent. bacteria.

The great influence that diet has upon the intestinal bacteria suggests that the best remedy for excessive bacterial action in the bowels is modification of the diet.

2. The percentage of bacteria in the feces of American subjects taken from hospital patients and normal persons of the more prosperous class—professional men and private patients—is lower than that given for Germans by Strasburger, who says that he finds that one-quarter to one-third of the dried weight of the stool is bacteria. This difference in our results is probably explained by the fact that the diet is not the same in the two sets of observations and in the two countries. Further investigations in America may show that classes of society who employ coarser foods may show a higher percentage of bacteria. In any event, the proportion of bacteria is probably higher than has been usually supposed, and this must be considered in estimating the total nitrogen of the stool. The presence of bacteria would furnish an amount of nitrogen that would lead to most confusing results in metabolic work unless the amount of bacteria present was determined and allowance made for this source of error.

*The bacteria are increased (a) in conditions in which there is excessive bacterial action in the stomach, such as achylia with diarrhea.* One such case showed 38 per cent.

The great influence of a modification of diet in restricting bacterial growth under these circumstances is shown by a case of carcinoma of the pylorus with partial obstruction, in a woman of sixty years. There was marked putrefactive and fermentative changes in the stomach with considerable retention, but not complete obstruction. Notwithstanding the number of microorganisms that must have escaped into the bowel through the pylorus the bacteria in the stool were but 3 per cent., showing that not enough food material came through the pylorus with them to permit of much bacterial growth. Later, when the pylorus became more patulous, probably through the separation of a slough, and the retention almost disappeared, the bacteria rose to 22 per cent.

(b) In two cases of *hyperacidity*, one with diarrhea, the bacteria went as high as 28.5 per cent. on a hyperacidity diet, containing a large proportion of proteids and fat, and, consequently, with little residue. I believe this represents a high proportion of bacteria for such a diet.



This increase in bacterial growth in hyperacidity may be due to insufficient starch digestion, or to the chemical irritation of the excess of HCl.

The reason why a chemical irritant that is in itself antiseptic may be associated with abundant bacterial growth in the intestine may be explained upon the assumption that anything that interferes with the normal functions of the bowel will probably disturb its inhibitory power upon bacterial growth. Consequently an excess of HCl may favor bacterial growth for the reasons just given.

(c) Poor *starch digestion* in one case gave 27 per cent. When the starch of the diet was reduced in quantity to one-half of what it had been, the bacteria fell to 14 per cent. The reaction of the stool in this case was strongly acid.

(d) The bacteria were increased in one case of chronic cholecystitis, 38 per cent. (full diet); one case of gumma of the pancreas, 22 per cent. (liquid diet). Both of these diagnoses were confirmed by operation. Two cases of intestinal indigestion showed a high proportion of bacteria.

(e) The growth of the intestinal bacteria is increased by the administration of various of the so-called *intestinal antiseptics*.

*The intestinal bacteria are decreased in amount* in (a) diets leaving small residues for reasons given above.

(b) In uncomplicated *constipation*, usually spoken of as atonic.

Schmidt and Strasburger have shown that in uncomplicated constipation the ingested food is too thoroughly absorbed in its passage through the gastro-intestinal tract; consequently, very little residue is left upon which the intestinal bacteria may grow and, as a result, the proportion of bacteria in the feces is reduced to 10 per cent. or under. Schmidt suggests that the products of bacterial action, such as gases and various aromatic substances, may be a necessary stimulant for the normal activity of the intestinal muscle, and when this is absent constipation results. I am inclined to agree with Schmidt that certain forms of constipation may be caused in this manner.

Other cases of constipation show no diminution, but an increase of bacteria.

(c) *The intestinal bacteria are not increased in jaundice*. If the older idea and teaching was true, that bile is an antiseptic and that one of its functions is to prevent excessive bacterial activity in the intestine, then we should expect the bacteria to grow more luxuriantly when bile is absent from the intestine. This is not the case, however.

In one case of gallstones and jaundice the bacteria were much diminished. This patient had jaundice; no bile in the stool; bacteria 2 per cent. (liquid diet). A week later there was some bile in the stool; bacteria 10.5 per cent. (semiliquid diet).

Strasburger says that in his case of simple jaundice the bacteria were very low. I am inclined to believe that the reduction in the bacteria in

jaundice occurs because the diet is usually reduced in such conditions, and not because the absence of bile inhibits bacterial growth.

(d) Certain intestinal antiseptics reduce the growth of the intestinal bacteria.

**THE TECHNIQUE OF THE METHOD.** The possibility of separating the bacteria from the rest of the feces depends upon the fact that the bacteria are so nearly of the same specific gravity as distilled water that they cannot be centrifugated out of a watery suspension of the feces, but remain suspended in the supernated fluid. Taking advantage of this, the bacteria can be removed by washing with the centrifuge. Then if the specific gravity of the wash water is lowered by the addition of large amounts of alcohol, the weight relation of the bacteria to the fluid is changed to such an extent that the microorganisms can be readily centrifugated out, separated, dried, and weighed.

Unless the period of passage of the feces has been ascertained to be normal, it is better to mark the beginning and end of each period of examination by carmine. The use of the Schmidt diet is not necessary. Indeed, I have found that this diet is not desirable because it leaves very little residue, and so of itself reduces the total amount of bacteria to a lower point than that which is usually found.

The whole stool is saved. Unless the feces are liquid they are rubbed up with a known amount of distilled water until they are smooth and semi-liquid and as homogeneous as it is possible to make them. This is a modification of my own, intended to make it easier to obtain a specimen of the stool that is fairly indicative of the average amount of bacteria contained in each cubic centimeter. Strasburger takes but 2 c.c. of the formed feces. It seems to me that since the different portions of the stool differs so in consistency and composition, this method of Strasburger leads to considerable error. I believe that my modification ensures a much more accurate idea of the average consistency of the stool.

Two portions of 5 c.c. are measured off with a pipette of large caliber. I use for this purpose an ordinary 5 c.c. pipette with the tapering end cut off, and with the necessary correction made at the mark. One of these portions of 5 c.c. is put into a porcelain dish and dried upon a water bath and later in a drying oven, in order to determine the dried weight. The addition of a little alcohol and thorough mixing will hasten the process of drying and prevent caking of the feces. The second portion is washed free from bacteria. This is done as follows: The wash water is 0.5 per cent. HCl solution in distilled water. The acid increases the solubility of the salts and soaps of the feces. I usually employ about 100 c.c. of this solution at the beginning of the washing. The feces are thoroughly mixed with the wash solution and then is centrifugated. The use of the water motor or electric centrifuge is almost essential. Each tube is centrifugated for about one and a half minutes; then the cloudy

supernatant liquid is poured through a layer of gauze. This fluid contains the bacteria in suspension. All of the mixture (the wash water and the feces) is centrifugated in the same way, and then the residue in the tubes is shaken up with more of the wash water and centrifugated again. This is repeated until the supernatant liquid after centrifugating is quite transparent, showing that approximately all the bacteria have been washed out. If a smear is made of the residue at this point, it will be found that the bacteria are not entirely washed away, but are evidently very much reduced. They occur singly, while in the unwashed feces they are in great lumps and masses. I do not believe that it is practicable or even possible to wash the feces entirely free from microorganisms.

Strasburger recommends that the wash water be centrifugated for a short time at high speed in order to remove any stray particles of solid residue from the suspension of bacteria. I believe this is a mistake, for if the decanting is carefully done in the first instance, then in my experience the sediment obtained with the second centrifugation is composed wholly of bacteria which would be lost if this part of the procedure was always carried out. The suspension of bacteria is then mixed with a liberal portion of alcohol and evaporated down slowly at a temperature of 40° to 50° C., until it amounts to not more than 50 c.c. in all. This takes approximately twenty-four hours. It is then mixed with at least twice its volume of alcohol, preferably absolute alcohol, although this is expensive and not absolutely necessary. This lowers the specific gravity of the fluid to such an extent that now the bacteria readily centrifugate out. The mixture is then centrifugated until the supernatant liquid is quite clear. This may take thirty minutes or more for each tube. The residue, which consists of the bacteria, is washed with pure alcohol and is shaken up with ether to remove the fat; then it is washed out again with alcohol. All of this washing is done by means of the centrifuge. The bacteria are next washed out of the tube with a little alcohol and evaporated to dryness, dried in the oven at moderate heat, dried in the desiccator, and weighed. Smears of the final preparation show that it consists of bacteria with a few very minute particles of other material. These particles are only visible with high power and are very few in number, perhaps two to each field of the  $\frac{1}{12}$  lens. They stain with methylene blue, and Strasburger suggests that they are cellulose, which they may well be. At any rate, the error arising from the inclusion of these small particles in the dried weight of the bacteria must be very small, and is probably balanced by the bacteria that it is not possible to wash out of the residue in the first washing. During the preparation of the bacteria the first portion of 5 c.c. has been dried and weighed. We then know the dried weight of 5 c.c., the weight of the dried bacteria in 5 c.c., the original volume of the stool, and the volume after the addition of a known amount of water.

It is then easy to calculate the data that we desire, namely, the volume of the stool, its dried weight, the weight of the dried bacteria, and the percentage of bacteria in the dried weight.

**The Value of Intestinal Antiseptics.**<sup>1</sup> The value of antiseptic drugs has long been a subject of dispute. Some observers, especially the French, following Bouchard, have claimed much for such remedies. Other clinicians appear to have very little faith in their efficiency. In answer to these opinions, it may be said that antiseptic drugs have never been investigated in a thoroughly scientific manner, and perhaps it would be better to reserve our judgment until their action has been tested more thoroughly. If it can be proven that intestinal antiseptics, as a class, influence the growth of the intestinal bacteria, and especially if it can be shown in what manner they do this, then a definite place of more or less importance will be found for them in the therapy of gastro-intestinal disease.

One difficulty in determining their true value clinically lies in the fact that they are seldom given a comparative trial, but are used in connection with drainage of the bowel and stomach and regulation of the diet. Consequently, the action of the drugs is obscured, and ground is given for skepticism as to their value, because, of course, diet and drainage will usually do the work without the aid of drugs. The experimental observation upon their action has been inconclusive because no very comprehensive work has been done upon the subject, and the various observations that have been made have been somewhat contradictory.

It has been difficult to find a satisfactory index by which we can measure directly the effect of a drug upon the intestinal bacteria. The chief methods that have been employed have been as follows:

1. Bouchard used the toxicity of the urine and feces as an index of the amount of auto-intoxication. This has some advantages, and at the same time certain disadvantages, one of which is that it is very hard to argue from the effect of a poison upon the smaller lower animals what its effect will be upon the human being.

2. The aromatic bodies in the urine have long been used as an index of the amount of absorption of products of intestinal putrefaction, and secondarily of the activity of the intestinal bacteria. It is now the opinion of those qualified to judge that the method is not reliable, either as an indication of the amount of intestinal putrefaction or of the absorption of bacterial products; especially it is incorrect as an indication of the action of antiseptics.

Alonzo Taylor<sup>2</sup> says: "Since we are not able at the present time to estimate or control the amount of aromatic derivatives eliminated in other forms than paired with sulphuric acid, it is obvious not only that

<sup>1</sup> See paper by J. D. Steele, Transactions of the Association of American Physicians, 1907.

<sup>2</sup> Osler's Modern Medicine, vol. i, p. 275.

the estimation of indican must often be of no value, but also that the estimation of the conjugated sulphates must often yield an uninterpretable result, and one that will permit of no inference as to the degree of intestinal putrefaction."

There are several methods of directly observing the effect of drugs upon the intestinal bacteria: The living bacteria may be counted by plating a known quantity of feces in agar. A large number of bacteria that are present in the small bowel and upper colon die before they are passed in the feces, and consequently such observations must be made by obtaining the feces from a fistula at the lower end of the ileum. This has the advantage that it shows the effect of the antiseptic directly upon the microorganisms at the point of their greatest activity, but the disadvantage that simple plating in one culture medium will not detect all the bacteria in the feces, especially the anaërobic varieties. Moreover, only a small portion of the matter is examined, and the feces are far from being homogeneous. The necessity of a fecal fistula, too, limits the field of investigation, especially in the human being.

Schuetz observed the action of various drugs by passing certain easily recognized saprophytic bacteria through the bowel, and noting the number of them that passed through alive during the administration of the different antiseptics.

The method of Strasburger measures the whole amount of bacteria in the stool, dead as well as living. The process has elements of technical error, but they are small, and if the results are considered in a comparative manner, and are regarded to some extent in round numbers, then I believe that the estimation of bacteria by weight is a good index of general bacterial activity in the intestine, and of the action of the various remedies used to influence the bacteria.

When the method is used as an index of the action of intestinal antiseptics in normal persons with good digestion, it is very difficult to determine whether putrefactive or fermentative bacteria are most affected. For the present we must be content with an idea of the action of such drugs upon the bacteria as a whole; and for this purpose I believe that Strasburger's method is an advance over any used heretofore.

**THE ACTION OF ANTISEPTIC DRUGS UPON THE INTESTINE.** An ideal intestinal antiseptic should have the following properties: (1) It should not be toxic if absorbed. (2) It must be easily diffusible through the intestinal contents. (3) If intended for the intestine it must not be destroyed by the gastric secretion or must be given in a covering that is resistant to hydrochloric acid. (4) It must not be too irritating to the intestinal mucous membrane.

The work of Schuetz indicates that the intestine has some power of self-protection against saprophytic bacteria introduced through a duodenal fistula, and as the intestinal juices did not affect the growth of

the bacteria in vitro, Schuetz concluded that the power probably lay in the intestinal wall and was biological in character.

As I have said, it seems probable that the normal activity of the colon bacilli in the intestine inhibits the growth of certain less desirable micro-organisms, and so the colon bacilli contribute to the self-protective power of the healthy intestine. Theoretically, any substance that would irritate the intestinal wall to such an extent as to interfere with its function or would disturb the proper relation between the colon bacilli and the rest of the intestinal flora, might interfere with this power of self-protection, and the increase in bacteria due to the withdrawal of the normal inhibitory influence of the intestine might then far overbalance the action of the antiseptic. In such cases the intestinal bacteria would apparently be increased by the antiseptic instead of diminished. It may be that the discrepancies in the results obtained in the investigations of various observers can be explained in this way. It will be seen from reference to the following summary how conflicting these different observations have been:

Stern found that bacteria gradually died out in some calomel stools which were allowed to stand for several days. In other calomel stools this did not take place.

Von Mieczkowski found that menthol and tannopin given by the mouth diminished the number of colonies in specimens of feces taken from a fistula at the lower end of the ileum, while with itrol and bismuth the results were negative.

Schuetz introduced a culture of *Vibrio Metschnikoff* into a duodenal fistula, and observed the number of these bacteria recovered alive in the stools. Castor oil did not influence the microorganisms. Calomel in large doses increased the number that came through alive.

Schönenborn used Strasburger's method as an index. He found that naphthalene (2 grams daily), itrol (0.3 gram daily), thymol (1.5 grams daily), increased the bacteria, and that salicylic acid mixed with the food diminished them.

Hoffman found that isoform given by the mouth diminished the number of colonies in the feces obtained from an iliac fistula.

Bouchard found that naphthalene, iodoform, and charcoal diminished the toxicity of the urine and stools.

Herter says that salicylates given as aspirin or salol have in his experience exerted some action in diminishing the output of the indican.

My own observations were undertaken in order to attempt to answer the fundamental question upon which all investigations of intestinal antiseptics must rest, namely, whether it is possible to influence bacterial growth in the intestine of normal subjects by antiseptic drugs given through the mouth. To do this I have used Strasburger's method as an index. Subjects upon which the experiment is made should be normal, because in them it is possible to exclude the variations in the amount of

bacteria that may take place during the experiment due to the diseased condition and not to the drug. No systematic work of this sort, so far as I know, has ever been done. The two antiseptics employed were chosen because they fairly represent two important classes of such remedies, and both are known to possess decided antiseptic power.

*Bismuth salicylate* is non-irritating, and is one of the drugs that depend upon salicylic acid for its activity, which substance has been generally regarded as one of the best preparations for disinfection of the gastro-intestinal tract. *Beta-naphthol*, on the other hand, belongs to the more irritating and toxic class of such remedies.

The subjects that I chose for my observations were, with one exception, without intestinal symptoms, or any signs of intestinal disease.

The drugs were from reliable manufacturers and were given in capsules. Every effort was made, and I believe with success, to keep the subjects under the same physical conditions in all the stages of the experiments.

The diet employed in 3 of the cases was that known as full hospital diet, in which the three main constituents were fairly well balanced, and there was certainly no excess of meat. One of the other cases was upon a full home diet, also well balanced, and the last case was upon the so-called soft diet of the hospital.

The amount of bacteria passed varies from day to day with the amount of the stool and other factors. Consequently, all of my comparisons have been made by obtaining daily averages of the stools for three or four days.

First, a control observation was made for several days without drugs, and then the result of this was compared with the daily average of a similar period after the drug had been given for several days. The results were quite conclusive and may be summarized as follows:

1. In the 3 cases in which bismuth salicylate was used the daily average amount of bacteria fell within three days after the drug was given, to one-half or one-quarter of what it was in the control observation.

2. In 2 cases in which beta-naphthol was given the bacteria fell after three days to about one-half of the control.

3. In the third beta-naphthol case the bacteria increased for three days, and then remained about the same as the control for three days. This was the only patient in which there were gastro-intestinal symptoms. She was a young woman with gastroptosis and insufficient gastric secretion, and with symptoms of intestinal disturbance.

This indicates that we must not assume, without further investigation, that the action of the drugs will be the same in a diseased bowel as in a healthy one. The variations in the results thus far obtained suggest very strongly that there is some important factor involved that we do not understand. This may be the natural self-protective power of the intestinal wall as suggested by Schuetz, or it may be the antagonism between the colon bacilli and other microorganisms, or it may be some other agency.

At all events, our investigations show that while antiseptic drugs have the power to check bacterial growth under some circumstances, under others they seem to have no effect, and sometimes they even increase bacterial activity. So it may well be that antiseptic drugs will act differently in intestines in which the function of the mucous membrane are disturbed than they will act under normal conditions. The failure of the beta-naphthol to reduce bacterial growth in the case of indigestion may be an instance of this—that is, the intestinal mucous membrane was more easily irritated than in the healthy subjects, and its self-protective power was impaired; consequently, the beta-naphthol did more harm to the intestine than to the bacteria, and hence bacterial activity was increased.

On the other hand, I found that bacterial growth in the intestine was decidedly diminished in normal subjects during the administration by the mouth of two typical intestinal antiseptics, and I think that this is evidence in support of the belief that it is possible to check bacterial activity in the normal intestine by antiseptic drugs.

The whole subject needs much more thorough investigation, which I hope to give it in the future. At the present time, it seems highly probable that, as a rule, the so-called intestinal antiseptics do more harm than good in diseased states of the gastro-intestinal tract.

Still, the fact remains that under normal conditions such drugs certainly have a very powerful effect in diminishing bacterial activity in the intestine, as measured by the total bacteria of the feces, and it may be possible that there are some conditions of disease in which their action will be of benefit.

In conclusion, I wish to say that I am firmly of the opinion that evacuation of the intestinal contents, combined with regulation of the diet, are by far the most efficient means at our command to check excessive bacterial activity in the intestines.

In my observations upon the amount of intestinal bacteria, I have been impressed again and again by the important part that diet plays in influencing bacterial growth. I have made no comparative study of the effects of different foods, but I have no doubt from what I have seen in my work that by regulating the amount and character of the food ingested, we have the strongest and surest means of checking excessive bacterial activity in the intestines.

**Intestinal Disease Associated with Eosinophilia.** The diseases of the mucous membrane associated with eosinophilia are characterized, as we have learned in bronchial asthma, (1) by the presence at the point of disease of eosinophilia, (2) by the local occurrence of Charcot-Leyden crystals in close association with the eosinophilic cells, and (3) by increase in the eosinophilic leukocytes in the blood.

The evidence at hand is strongly in favor of the theory that the Charcot-Leyden crystals are formed from the eosinophilic granulations of the leukocytes, and consequently their appearance has the same significance



as the presence of the eosinophiles. Increase in the percentage of eosinophiles in the blood is a frequent but not constant part of the symptom complex.

The best known eosinophilic diseases of the bowel are, of course, those associated with animal parasites. Eosinophiles were described in the bowel first in ankylostomiasis and afterward with other parasites. The crystals are common in the stools, for the eosinophilic leukocytes quickly degenerate in the intestinal contents.

Some attempts have been made to establish the presence of eosinophilia and Charcot-Leyden crystals in the intestinal contents as a pathognomonic sign of certain parasites, especially the ankylostoma and auguillula, but later investigators have shown that such findings in the intestinal contents are characteristic not only of most animal parasites, but of other diseases as well. Thus, George Dock and Musser and myself have found eosinophiles in the bowel contents and eosinophilia in the blood in amebic dysentery.

Nothnagel and Akerlund have found eosinophilia in different diseases of the intestines not parasitic. Neubauer and Stäubli,<sup>1</sup> working in F. Müller's clinic, have collected a series of cases which show that eosinophilia may be associated with a variety of non-parasitic inflammatory diseases of the intestines.

The first describes 2 cases of gastro-enteritis with large numbers of Charcot-Leyden crystals and eosinophilic cells in the stool, but with no increase of eosinophiles in the circulating blood. A case of acute dysentery in which no ameba or Shiga bacilli were found showed eosinophiles and crystals in the stool, but no eosinophilia of the blood.

Neubauer and Stäubli describe a condition of the rectum which they call exudative eosinophilic proctotitis. The proctoscope showed that the rectum was congested and the rectal mucous membrane was thickly covered with small outgrowths the size of a linseed or pea. These outgrowths were yellow and soft and microscopically consist of eosinophilic leukocytes, granulation tissue, and Charcot-Leyden crystals. The removal of the exudate leaves an abrasion which bleeds very easily, but no deep ulcers or scars were ever observed.

They describe 3 cases of this condition. They were all young people, who suffered from diarrhea and mucous and bloody discharges. In 1 case the loss of blood was so great as to cause a severe anemia. The stools were frequent, watery, and contained visible blood and mucus.

In 3 cases Charcot-Leyden crystals were found and in 2 eosinophiles in the stools. No animal parasites or their eggs or specific bacteria (dysentery, tubercle bacilli, or gonococci) were found. In 2 of the 3 cases the eosinophiles were increased in the circulating blood.

The disease may begin suddenly and the attack may last for weeks and

<sup>1</sup> Münchener med. Wochenschrift, 1906, liii, Nr. 49.

months and then disappear almost entirely, to relapse after a certain length of time.

Neubauer and Stäubli draw some parallel between the condition and bronchial asthma.

**The Recognition and Occurrence of "Lost Albumin" in the Feces.** Schloessmann<sup>1</sup> used the method of Ury with some modifications of his own in determining the amount and character of the albuminous bodies in the feces. The stool is mixed with water; after a few hours it is filtered through a double filter and the cloudy fluid is clarified by means of silicon. The nucleoproteids are precipitated by acetic acid and then the mixture is refiltered. The filtrate is then tested for other forms of albumin. With the exception of the mucin bodies the occurrence of nucleoproteids in the feces is rare. In the fresh feces it is possible to obtain a weak reducing, mucin body. Excessive ingestion of nucleoproteid, as a rule, does not show in the feces, except in children, where its occurrence is more common.

Under pathological conditions the nucleoproteids may be decidedly increased, although their presence is not characteristic of any particular disease. Other forms of albumin are rarely found in the feces even after the ingestion of excessive amounts. Again, an exception to this is found in childhood, when the occurrence of albumin in the stool is more common without any apparent alteration in the functions of the bowel. The occurrence of albumin in the feces of adults is almost always associated with diarrhea and usually with an excessive formation of mucus. It usually is serum albumin, much less frequently albumoses. Such "lost albumins" in the stool indicate severe anatomical changes in the bowel, but usually not disturbance of absorption. The albumins under these circumstances come from the intestinal wall, and sometimes a part of them may be digested by the intestinal ferments into albuminose.

The greater part of the ingested proteids are absorbed in the small bowel. As a rule, no proteid is found in the large bowel.

This work of Schloessmann throws a new light upon the significance of the presence of lost albumin in the feces. It was formerly thought to indicate imperfect digestion of proteids, but these observations would indicate that such is not the case.<sup>2</sup>

**True Intestinal Dyspepsia.** Einhorn<sup>3</sup> calls attention to his method of determining the functions of the intestines by the use of the so-called bead test,<sup>4</sup> and says that this method is more convenient and requires a shorter time than the test diet of Schmidt. Einhorn has modified the test since it was described in *PROGRESSIVE MEDICINE* of last year. He

<sup>1</sup> Zeitschrift f. klin. Medicin, 1906, Band lx, Heft 3 und 4.

<sup>2</sup> *PROGRESSIVE MEDICINE*, December, 1906.

<sup>3</sup> *American Journal of the Medical Sciences*, 1907. Read before the Gastro-enterological Association, 1907.

<sup>4</sup> *PROGRESSIVE MEDICINE*, December, 1906.

now connects all the beads with a thread and thus makes certain that they all come through together. He refers to the functional achylia of the pancreas recently described by A. Schmidt and remarks that we have no well-tested means of measuring the functional activity of the pancreas. He has found the nucleus test unreliable and uncertain and agrees with a similar opinion that I ventured to express concerning it in *PROGRESSIVE MEDICINE*, December, 1906.

After a long study of the intestinal functions by means of the bead test Einhorn is convinced that a very correct idea of the digestive functions of the bowel may be obtained by its use. Basing his studies of intestinal dyspepsia upon these observations, he concludes that it is possible to distinguish two large groups of intestinal disturbances:

1. Digestive disturbances which concern all three classes of food substances—namely, albuminates, carbohydrates, and fat. He calls this “*dyspepsia intestinalis universalis*.”

2. Digestive disturbances affecting only certain classes of food-stuffs—“*dyspepsia intestinalis partialis*.” This includes: (a) Disturbed digestion of proteids. (b) Disturbed digestion of carbohydrates. (c) Disturbed digestion of fats. (d) Disturbed digestion of two classes of food, such as proteids and carbohydrates, carbohydrates and fat, or proteids and fats.

These functional disturbances of the intestinal digestion may exist without appreciable anatomical change of the digestive apparatus or they may be associated with organic disease. Occasionally subjective disturbances are found in the intestinal tract in which neither anatomical nor functional deviations from the normal occur. Such cases may be considered true nervous dyspepsia. In using the bead test it must not be supposed that if one substance is undigested no digestion of that material occurs. The same food-stuff may be digestible if given in another form, but any failure of digestion indicates that there is some diminution in the power of the digestion.

Einhorn reports a series of cases illustrating the different forms of intestinal dyspepsia. He concludes from this study that complete intestinal dyspepsia may exist for a long time without necessarily endangering the life of the patient.

Under the second group, disturbances of carbohydrate digestion seems to be most common and indigestion of meat the rarest.

**TREATMENT OF INTESTINAL DYSPEPSIA.** Therapeutically, we can gather some valuable points as a result of such studies of the intestinal functions. For instance, in complete intestinal dyspepsia the patient must be given a liquid or semiliquid diet and, as medicines, pancreon and similar remedies.

In partial intestinal dyspepsia we can limit the amount of that sort of food that is not digested. Taka diastase in 5-grain doses three times daily is a valuable help in amylaceous dyspepsia and has removed the

subjective symptoms in several of Einhorn's cases. Pancreon in doses of 5 grains seems to work well in cases of proteid and fat indigestion, although the results are not so satisfactory.

**Idiopathic Dilatation of the Colon (Hirschsprung's Disease).** This condition, although much more frequent in children, also occurs in adults. Such a case is reported by J. Schreiber.<sup>1</sup> The patient was a woman, aged twenty years, in whom the symptoms first made their appearance three years previously. Obstinate constipation, enormous accumulation of gas, marked enlargement of the colon, and the absence of any obstructive cause led to the diagnosis of idiopathic dilatation of the colon. The direction of the peristaltic waves indicated that the transverse colon was the seat of the dilatation; but an *x*-ray picture, taken after the rectal injection of bismuth emulsion, showed that the sigmoid flexure was the part involved. The employment of diaphanoscopy confirmed this, and also indicated that it was the rectal limb of the sigmoid flexure. There was no local irritative process that could account for the spasm; hence, it must be regarded as an independent neurosis, analogous to that described by Fleiner and others as a cause of spastic constipation. This would seem to take the present case out of the class of Hirschsprung's disease, but the extraordinary position and length of the sigmoid flexure could only have been due to a congenital abnormality. This idiopathic abnormality, together with the essential spasm, combined to produce the enormous dilatation observed.

A remarkable feature of the case was the cure, which was rapidly effected by the use of opium. Under the influence of this drug the spasm became relaxed, the constipation was overcome, the dilated sigmoid returned to an approximation of its normal diameter, and the patient was restored to health.

## THE LIVER.

**Infections of the Biliary Tract.** A. O. J. Kelly<sup>2</sup> in the Mütter lectures of the College of Physicians of Philadelphia, 1905, gives a very complete summary of this important subject, and adds an analysis of 216 cases of biliary infections which he has observed clinically and pathologically in the German Hospital during the past six years. He says that the gross and obvious manifestations of such infections, namely, suppurative cholangitis, suppurative phlegmonous and gangrenous cholecystitis, and certain forms of abscess of the liver, were well recognized and described by our forefathers, but there are much more subtle infections of the biliary tract, illy understood, frequently overlooked, and commonly misinterpreted, because they give rise to no symptoms, at least no noteworthy symptoms for many years if at all. Indeed the symptomatology

<sup>1</sup> Arch. f. Verdauungskrankheiten, 1907, xiii, Heft 2, p. 101.

<sup>2</sup> American Journal of the Medical Sciences, 1906, cxxii, p. 446, 744.

of many of the varieties of such infection has not been worked out. These latent or masked infections form the basis of Kelly's paper. It is needless to point out the extreme importance of such conditions to the practitioner.

THE INFECTIOUS AGENTS were isolated in 70 cases. They were as follows:

	Cases.	Per cent.
Bacillus coli communis was found in . . . . .	23	32.8
Bacillus typhosus was found in . . . . .	7	10.0
Staphylococcus pyogenes aureus was found in . . . . .	2	2.9
Streptococcus pyogenes was found in . . . . .	1	1.4
Staphylococcus pyogenes albus was found in . . . . .	1	1.4
Bacillus coli and Staphylococcus aureus were found in . . . . .	2	2.9
No bacteria were found in . . . . .	34	48.6

THE PATHWAYS OF INFECTION. The diverticulum of Vater and the common bile ducts have long been looked upon as the most likely and the most common source of biliary infections, but whether with good reason remains to be decided. While it is probable that in a certain proportion the infecting agent enters the biliary passages from the intestine through the duodenal papilla there are some factors concerned in the mechanism of the process which have not yet been definitely determined. While we cannot deny that infection of the biliary passage may and probably does occur in some cases by way of the diverticulum of Vater we are forced to the conclusion (1) that certain ill-understood factors exercise in the process more or less unknown part and (2) that in the past we have unquestionably overestimated the importance and significance of this source of infection. The chief reasons of these statements are: (a) the sphincter of the diverticulum of Vater resists a pressure of 700 mm. of water from the intestinal side before allowing regurgitation (Oggi), and (b) the free flow of bile tends to wash clean the common duct.

Indeed it is doubtful whether an ascending infection ever occurs in the absence of stasis of the bile. The mechanical action of the bile in washing back material from the intestine is of course the important thing. The bile itself has no antiseptic power. Indeed it is a very good medium for bacterial growth. There is no reason why the bacteria should invade the bile ducts oftener than the pancreatic duct if they simply ascended from the intestine, and yet this seems to be the case. Also in cases of cholecystitis in typhoid the Bacilli coli should be found in the gall-bladder with the typhoid bacillus, while, as a rule, the typhoid bacillus is in pure culture.

*Infection by way of the portal circulation* is doubtless a common source of biliary infection, although it was for a long time overlooked. Definite experimental evidence has proven that the bile may be infected through the portal circulation (Lartigan, Blachstein, Welch, Sherrington, and others).

*Infection through the systemic circulation*, although not an exceedingly common channel of infection, should not be completely ignored. Its importance has increased since we have recognized the frequency, in fact almost the regularity in which bacteremia occurs in the great majority of infectious processes, such as typhoid, pneumococcic and pyogenic infections. Experimental evidence of the possibility of this form of infection has long ago been furnished by Welch and Blachstein and more recently by Doerr. The occurrence of cholecystitis and cholangitis as a complication of general infections is not infrequent and has been studied clinically by Richardson and Anders, and experimentally by Prior and Kayser.

*Infection by way of the lymphatic circulation and direct infection through the wall of the gall-bladder* are possible channels of entry for the microorganisms, but infection by these channels is certainly rare.

Kelly is inclined to believe that the frequency of gall-bladder infection in typhoid fever finds one of its explanations in that in typhoid all of the three sources whereby the biliary tract may become infected are present—although the systemic and the portal circulations are the more important.

Pneumococcic, pyococcic, influenzal infections, etc., are doubtless in many cases general systemic infections; in some cases the infection is probably by way of the diverticulum of Vater—but the subject still requires considerable elucidation.

**THE RESULTS OF BILIARY INFECTION.** The results of biliary infection vary with the virulence of the infecting microorganism and the resistance offered by the subject; they may be insidious or frank in onset, acute, subacute, or chronic in course, and slight or extremely severe in character. The frank acute cholangitis and cholecystitis are usually so obtrusive in their manifestations as scarcely to escape observation, and, although they sometimes present diagnostic difficulties, the disease is usually correctly recognized. When, however, the infection is more insidious in onset and subacute or chronic in course and the infecting microorganisms of low virulence, the resulting lesions are of such nature and the symptoms so slight or altogether absent that they are often illy understood, misinterpreted, and referred to organs other than their real source.

**LATENT OR MASKED INFECTIONS.** The introduction of microorganisms of low virulence into the biliary tract may be unattended by pathological lesions, and this is the more likely to be the case if the ducts are open and the flow of bile unobstructed. Comparatively virulent microorganisms also may sometimes be disposed of if the biliary drainage is free and unimpeded, but usually serious and fatal forms of disease are thus provoked—suppurative cholangitis and suppurative and gangrenous cholecystitis. Between the extremes of innocuousness or comparative innocuousness and quick and early disaster lie the great majority of cases of biliary infection.

As in other mucous canals, the immediate result of infection of the biliary tract is the production of a catarrh, with the usual inflammatory phenomena—edema and congestion of the mucous membrane, increased production of mucous, and desquamation of epithelium. If the biliary circulation is free and unimpeded the results of this catarrh are washed away for the most part, but on account of special local conditions (largely mechanical) they are likely to accumulate, to become accentuated, and to persist in the gall-bladder. In the event of obstruction to the free flow of bile these are all the more certain to occur. In many cases the lesions thus provoked are entirely latent or unannounced by noteworthy symptoms; they may pursue a short course, or they may continue for years; and they are one of the most important factors, in fact, the important factor, in the etiology of gallstones. These latent or masked infections are doubtless due to different microorganisms in different cases, but since a large majority of them are due to the typhoid bacillus (and its brother the paratyphoid bacillus) they may be studied from the point of view of typhoid infections.

**TYPHOID INFECTION.** We know the following facts concerning the biliary passages in typhoid with fair certainty:

(1) That the typhoid bacillus is regularly present in the gall-bladder, and commonly in pure culture, in practically all cases of typhoid fever—indeed, it is the one region of the body from which a pure culture of the organism is most likely to be obtained. (2) That the typhoid bacillus may persist in the gall-bladder, as well as within gallstones, weeks, months, even years, after the patient has recovered from an attack of typhoid fever. (3) That cholangitis and cholecystitis (catarrhal, suppurative, and gangrenous) are by no means infrequent complications of typhoid fever. (4) That a history of antecedent typhoid fever may be obtained in many cholecystitic subjects. Furthermore, it is important to bear in mind, as has recently been insisted upon by Doerr, Forster and Kayser, Brion and Kayser, and also by Kelly himself, that many of these subjects—some apparently healthy and others ill only with a local disorder—are unconscious harborers and disseminators of the typhoid bacillus.

The continuous reinfection of the intestinal tract by the frequent discharge of virulent typhoid bacilli from a chronically infected gall-bladder may be of much significance to the individual, but it is of even more significance from the epidemiological point of view—since there can be little doubt that these apparently healthy harborers of typhoid bacilli spread the infection and sometimes may even give rise to more or less extensive epidemics.

What Kelly emphasizes, however, is the fact that in many cases the biliary infection though present is altogether latent clinically, and that although in other cases it occasions demonstrable symptoms, the true nature of these is often masked and they escape correct interpretation.

*The different manifestations of typhoid infection are as follows:* First, there are cases in which, during the course of typhoid fever a noteworthy enlargement of the gall-bladder occurs: but the biliary ducts are open, and the drainage is therefore sufficient, and the patient's sensibilities being somewhat obtunded, there is no complaint. Consequently the disorder escapes clinical recognition—unless perchance systematic and repeated examinations of the gall-bladder region are undertaken; in this event a more or less enlarged and tender gall-bladder may be encountered. It is really surprising how frequently this occurs, and Kelly suggests that it is surprising how frequently it goes undetected. Second, there are cases in which a little epigastric discomfort, perhaps slight nausea, in some cases actual pain, is complained of, and examination reveals an enlarged and tender gall-bladder. Kelly has come to regard nausea during the course of typhoid fever, when not due to other obvious cause, as quite significant of gall-bladder infection, although, of course, it may be due to other factors. Third, there are cases in which an acute cholecystitis or cholangitis develops—often severe in type. This is probably more common during or after convalescence than during the course of the infection.

*The Relation of Relapse in Typhoid Fever to Biliary Infections.* Kelly points out the significant fact that in reality many of the so-called relapses in typhoid fever are by no means relapses in a restricted sense, but rather manifestations of some local infection of the body—often of the biliary tract. In many cases a gall-bladder infection will be found; in other cases, an infection of the urinary tract; in others, fecal impaction, furunculosis, osteitis, periostitis, etc., while in still other cases the increased flow of infected bile occasioned by a return to a liberal diet, or other factors, may determine what may be looked upon as a real relapse—commonly reinfection from an infected gall-bladder. But in most cases persistent search for a local infection will be rewarded with success. These, especially the gall-bladder infections, have important surgical bearings, and should be attentively studied. It is true that the inflammatory phenomena frequently subside spontaneously and the indication for surgical intervention passes away, but these infections are a fruitful source of mischief in later life—often causing gallstones, subacute and chronic cholecystitis, pericholecystitic adhesions, and other symptoms that commonly are grouped under the general term of "stomach trouble."

Doubtless bacteriological investigation of the stools of chronic cholecystitis subjects would frequently disclose the typhoid bacillus.

*The Gruber-Widal Reaction in Cases of Jaundice.* Since the earliest days of the clinical use of the Gruber-Widal reaction in the diagnosis of typhoid fever, cases of so-called catarrhal (as well as other forms of) jaundice have been observed in which the serum reaction was positive—whence at first it was not unnaturally thought that possibly jaundice



vitiating the diagnostic trustworthiness of the serum reaction. However, since we have come to recognize the importance and the frequency of typhoid infection of the biliary tract, and since we have learned of the occurrence of a primary typhoid cholecystitis and cholangitis, we have come also to think that these cases of jaundice are examples of typhoid infection, and that the Gruber-Widal reaction is of much importance in determining the nature of the jaundice.

In a number of cases of jaundice that have yielded a positive Gruber-Widal reaction the typhoid bacillus has been isolated from the biliary tract at operation or after death; and since it has been determined experimentally that the bile as such has little if any tendency to cause agglutination of the typhoid bacillus, it is only reasonable to look upon a positive serum reaction in cases of jaundice as evidence of typhoid infection of the biliary tract.

There can be little doubt that we have much to learn of the nature of certain ill-understood forms of jaundice—so-called febrile jaundice, infectious jaundice, Weil's disease, etc. The resemblance that many of these cases bear to typhoid fever has been frequently commented upon, and it has in fact been suggested that Weil's disease is in reality a modified form of typhoid fever. Possibly in many cases it is only typhoid infection of the biliary tract. That this may well be so is suggested by the extreme variability of the known lesions of typhoid infection of the biliary tract, from mildest local catarrhal lesions to widespread and fatal suppurative cholecystitis, cholangitis, and multiple abscesses of the liver. Furthermore, it is interesting to bear in mind that jaundice sometimes occurs at the onset of typhoid fever, as in some cases reported by Ogilvie and others, and that epidemics of so-called catarrhal jaundice are occasionally observed.

**THE FORMATION OF GALLSTONES.** There is general agreement that the one necessary factor in the causation of gallstones is a low-grade catarrhal inflammation of the biliary tract; the second requisite seems to be some obstruction to the free flow of bile. The one without the other factor is not sufficient: whether a third factor is of significance remains to be determined. As a consequence of bacterial infection of the biliary tract a low-grade catarrhal inflammation is set up; this leads to obstruction to the free flow of bile from swelling of the mucous membrane and the products of this inflammation, and the retained bile contains the essential constituents of gallstones. In the gall-bladder (the seat of formation of most gallstones) the catarrhal inflammation leads to desquamation of the lining epithelium, an albuminous exudation, and an increased formation of mucus and of cholesterin, and in the gall-bladder dynamic factors doubtless frequently favor the stagnation of bile. The increased cholesterin, then, is not derived from the bile (being, according to Naunyn, independent of general bodily and diathetic conditions), but results from catarrhal disintegration of the mucous cells lining the wall

of the gall-bladder. An early evidence of this increased formation of cholesterin may be seen microscopically in the so-called myelin droplets or bodies within the mucous cells. The second important constituent of the gallstone, bilirubin-calcium, is derived from the bile, being precipitated by the albuminous exudation of the inflammatory process—a phenomenon that can be imitated experimentally by adding egg albumen to normal bile.

Stagnation and inspissation of the bile, to which, according to the older views, the formation of the gallstones was due, do not give rise to the increased formation of cholesterin nor to the precipitation of bilirubin-calcium, whence they are contributing factors only. Bilirubin-calcium is believed by Naunyn to act as a cement substance binding together the cholesterin, desquamated epithelium, etc., the whole forming the nucleus of the gallstones. The exact significance of foreign bodies and of chemical substance apart from bacterial products has not yet been definitely determined. There being no cholesterin-bearing mucous membrane in the smaller bile ducts, cholesterin gallstones are not formed within the intrahepatic ducts, although by a retrograde movement they may be transported thither; bilirubin-calcium calculi only are formed in the intrahepatic ducts; but both varieties, as well as mixed calculi, are formed within the gall-bladder.

Whether infection and obstruction to the free flow of bile comprise all the necessary factors in the causation of gallstones remains to be definitely determined; but there is some reason for concurring with Herter when he says: "It is plain from what has been said that there is at present no unequivocal evidence that gallstones arise from constitutional derangements unconnected with microörganismal invasions of the gall-bladder. On the other hand, it is certain that the cholesterin of the bile can be considerably increased by local irritants unconnected with infection, and it is likely that the requisite local conditions for such increase sometimes arise through purely metabolic disorders. While gallstones are commonly the result of local infections, we should carefully guard against the conclusion that they can never have a diathetic origin. It is at least highly probable that diathetic conditions are capable of so altering the composition of the bile as to favor materially the production of calculi in the presence of suitable local bacteria activities."

Beer has also recently suggested that a third factor which, he says, may be called altered liver metabolism or a diathesis, may be of significance in the etiology of gallstones. He believes that Naunyn's factors, stagnation of bile and inflammation of the biliary passages, do not seem to be sufficient in themselves to lead to gallstone formation, even though the time allowed for the working of the causes be adequate, and that these factors lead to gallstones only in persons who previously have had gallstones.

We may conclude, however, that at least the great majority if not all

gallstones have a bacterial origin and arise in consequence of some form of infection of the biliary tract.

*The Symptoms of Gallstones.* The consequences of gallstone activity may be mechanical or inflammatory or both. The mechanical consequences follow what may be designated wandering of the stone into and through the biliary passages. In consequence of this activity, the gallstone may set up mechanical effects in the gall-bladder, in the cystic duct, in the hepatic duct, in the common bile duct, in the diverticulum of Vater, or in the intestine. These effects are of great variety and of varying importance. Probably the most important and serious comprise permanent complete obstruction of the common bile duct, with consequent permanent jaundice, dilatation of the bile ducts, and final biliary cirrhosis of the liver. Of only less importance are the dragging sensations and discomfort attendant upon the weight of many gallstones in a distended gall-bladder; the gradual production of a Riedel or a linguiform lobe of the liver; the effects of pressure on adjacent organs; complete obstruction of the cystic duct which, as a rule, leads at first to some distention of the gall-bladder, but soon to absorption of the bile and its replacement by mucus (hydrops) and gradual shrinkage of the gall-bladder, etc. These and other mechanical consequences of gallstone activity, however, especially incomplete obstruction of the ducts, acquire most of their importance from the opportunity that they afford for bacterial infection; in fact, they invite such infection, and the infection is usually a concomitant condition.

This infection of the biliary tract is of the utmost significance, and forms an integral part of what is commonly designated calculous cholecystitis and cholangitis. The phenomena may develop (1) acutely, without preceding clinical signs referable to the gall-bladder; (2) subacutely, and (3) chronically. The ensuing pathological lesions are of the greatest diversity. Thus, for instance, (a) gallstones may or may not be present, and the concomitant inflammatory phenomena may be of varying grades—from the mildest catarrhal lesions to widespread phlegmonous and ulcerative processes that may lead to perforation or gangrene of the gall-bladder; (b) gallstones, if present, may be quiescent or active; they may be present in the gall-bladder, or in any one of the ducts, or in all the ducts, or in the ducts and not in the gall-bladder; they may cause an acute or chronic, partial or complete, temporary or permanent obstruction of the cystic, the hepatic, or the common bile ducts; (c) on the other hand, such obstruction may occur in the absence of gallstones, being due to swelling of the mucous membrane, kinking of the ducts, or obstruction from without; (d) in the presence of gallstones the ducts may be partially or completely patulous; (e) the gall-bladder may be distended or contracted, its walls thinned or much thickened and its lumen ultimately may become almost if not quite obliterated; it may contain bile, mucus, blood, or pus, or combinations of these; (f) adhe-

sions may form between the gall-bladder and adjacent structures (the liver, the stomach, the duodenum, the colon, the omentum, etc.), and by way of the adhesions, the gallstones may rupture into the gastrointestinal tract and sometimes cause intestinal obstruction; or purulent pericholecystitis and pericholangitis, localized or generalized peritonitis, pylephlebitis, pericholangitic abscesses of the liver, or fistulæ; (g) acute and chronic pancreatitis, etc., may ensue; and (h) finally, in some cases a general bacterial, often pyococcic infection, with or without multiple abscesses, may develop.

*The Pain in Gallstone Disease.* In Kelly's series 216 patients had gallstones: 74 per cent. had colicky pain; 85 per cent. of these had gallstones; 21 per cent. had pain not colicky; 77 per cent. of these had gallstones; 3 patients had no pain at all; 2 of these had gallstones; 1 was jaundiced and the other 2 had intermittent fever.

The weight of evidence at hand strongly suggests that the presence or absence of pain is determined not by the presence of stones alone, but by the presence or absence of an acute infection of the biliary tract; that is, an exacerbation of a cholecystitis or cholangitis is the factor that causes a quiescent process to become painful. Even the non-colicky pains are probably due to inflammatory phenomena provoked by infection, producing inflammation of and about the gall-bladder and bile ducts. The dull, aching pains are best ascribed to inflammation and subsequent distention of the gall-bladder, and the more acute pains associated with tenderness and muscular rigidity are due to involvement of the peritoneum, which in turn produces adhesions about the gall-bladder.

Kelly emphasizes the point that considerable distention may occur without pain provided the gall-ducts are patulous. This is probably the reason why the gall-bladder may be enlarged and tender in typhoid, and yet there may be no spontaneous pain. The referred pain (to the epigastrium, subscapular region, neck, shoulders, arms, etc.) is best explained by remembering that the pneumogastric nerve distributes filaments to the gall-bladder. And this is why cardiac and stomach symptoms are frequently associated with gall-bladder disease. The occurrence of pain, sometimes of actual colic, three or four hours after a meal in these gall-bladder cases may be due to the reflex contraction of the gall-bladder, due to the entrance of chyme into the intestine from the stomach.

Kelly is decidedly of the opinion that we have been too ready to regard colicky pains as due entirely to the passage of a gallstone through the ducts. Such pains may be due to other conditions as well, as pointed out by Reidel—namely: (1) Adhesions of a gall-bladder no longer containing stones; (2) adhesions when large stones are present in the gall-bladder and the cystic duct is patent; (3) inflammatory processes in a gall-bladder distended by fluid or stones when the cystic duct is occluded by.

inflammation or by the presence of a stone in the neck of the gall-bladder; (4) the transit of a stone through the bile passages, and (5) the inflammation of a dilated, calculous common duct, or its tributaries, without impaction of the stone.

There can be little doubt that in a number of cases the spasmodic efforts of the gall-bladder and the common duct to expel their contents by vigorous contraction of their muscular coats are the cause of the peculiar gallstone colic. This pain occurs in its greatest intensity during the transit of a stone through the ducts and it ceases as the stone is discharged into the intestine or drops back into the gall-bladder, thus freeing the cystic duct. But there can also be little doubt that attacks of pain indistinguishable from those provoked by the transit of a stone may be due to other factors—those mentioned above; although in some instances the attacks of pain may not be as severe as those of a so-called true gallstone colic. We should, therefore, interpret the great majority of gallstone colics, not as evidence of the passage of a stone through the biliary ducts, but as evidence of an acute cholecystitis. A fact tending to support this view is that as the inflammation subsides the stones become quiescent; indeed, the one hope of medical treatment is to cause subsidence of the infection and inflammation.

*Jaundice in Gallstone Disease.* In a general way we may say that jaundice may be due to one of two factors: (1) Mechanical obstruction of the biliary passages and (2) some disturbance in the bile-secreting function of the liver. The mechanical obstructions comprise (a) those due to a gallstone, (b) those due to inflammatory swelling of the lining of the biliary ducts, and (c) those due to compression of the common duct or of the extrahepatic part of the hepatic duct by a large stone in the cystic duct, swollen lymph glands, regional tumors, inflammatory exudations, adhesions, kinking of the ducts, etc. We may, therefore, speak of a lithogenous jaundice, an inflammatory (or infectious jaundice) and a compression jaundice, illy advised as these terms may be on some occasions. The practical deductions to be drawn from the known facts are: (1) that in some cases of cholelithiasis jaundice is not due to obstruction of the ducts by a stone, but rather to infection and inflammation of the ducts, and (2) that in many cases of cholelithiasis jaundice does not occur at all, although other important and other distressing symptoms may be quite obtrusive. In Kelly's list of 216 patients, 74 (34.2 per cent.) never had jaundice, 141 (65.3 per cent.) had no jaundice at the time of operation, whereas 121 (56 per cent.) gave a history of attacks of jaundice prior to the time of operation. The jaundice in some cases antedated the operation many years; in some cases long periods of freedom from jaundice followed; in some cases there were no subsequent attacks of jaundice whatever after the first attacks. Remembering, then, that jaundice may be entirely absent and that when it occurs it may be late, inconstant, and inconspicuous, we should train ourselves to recognize

cholecystitis and cholelithiasis in the absence of jaundice and of gall-stone colic.

*The Size of the Gall-bladder in Gallstone Disease.* The clinical significance of the size of the gall-bladder has engaged the attention of physicians and surgeons for a long time, but special consideration has been given to its diagnostic importance since a knowledge of what is known as Courvoisier's law has become general. As is well known, Courvoisier, basing his opinion upon an analysis of 187 cases, stated that in cases of chronic jaundice contraction of the gall-bladder is suggestive of gallstones, and that dilatation of the gall-bladder is suggestive of biliary obstruction caused by factors other than gallstones—that is, pressure from without, most often carcinoma of the head of the pancreas. This so-called law is generally made use of nowadays in diagnosis, and serves us well in the majority of cases, although, as Courvoisier himself admitted, there are some notable exceptions to its universal applicability. Thus in 40.5 per cent. of 116 patients of Kelly's list that had gallstones and jaundice the gall-bladder was enlarged. In somewhat more than one-half of these cases, however, the gallstones were present in the gall-bladder alone, and the associated jaundice was doubtless due to inflammatory swelling, pressure from without, etc.

Kelly does not, therefore, call into question the general trustworthiness of Courvoisier's law—of the value of which there is ample corroborative testimony—but suggests the value of continued study of the conditions found at operation, and emphasizes the importance of basing our diagnoses upon the varying grouping of the symptoms in the different cases, rather than upon any single symptom or sign.

When the gall-bladder becomes thickened and hardened from long-continued inflammation it is manifestly impossible that it should dilate, no matter what obstruction there may be in the common duct. And, on the other hand, it is quite conceivable that there may be certain conditions associated with gallstones that would cause dilatation of the gall-bladder and jaundice. The practical inference is that, although, as maintained by Courvoisier, his law may hold good in 80 per cent. of cases, a patient with chronic jaundice and enlargement of the gall-bladder should not be unceremoniously condemned to the diagnosis of carcinoma of the pancreas, but that the grouping of the other symptoms should determine the diagnosis and suggest the treatment.

*The Fever in Gallstone Disease* is always a symptom of the infection and is not due to reflex causes—nervous or otherwise—as was formerly taught.

*Adhesions of the Upper Abdomen.* Kelly points out the importance of adhesions in the region of the gall-bladder and bile-ducts. This is a most interesting and practical subject and one that is attracting considerable attention at present

These adhesions have frequently been encountered by pathologists

and surgeons, but it is only recently that we are awakening to a knowledge of their full import. Their production is intimately associated with inflammatory phenomena of the organs of the upper abdomen—the gall-bladder, the biliary ducts, the stomach, the duodenum, etc.; but, of all organs, the biliary tract is the chief offender. In most cases these adhesions represent the sequels of past subacute and chronic, sometimes acute, inflammation of the organs hereabout, and they are thus a direct result, an expression, of infection.

The conditions are quite analogous to those in and about the vermiform appendix. Should the biliary infection be acute and virulent, the bacteria or toxins penetrate the wall of the gall-bladder or the biliary ducts and engender a fibrinous exudation, a more or less local peritonitis. In the event of later development of suggestive clinical symptoms, much diagnostic significance attaches to a history of such past infections (typhoid fever, definite cholecystitis, etc.).

In the subacute and chronic infections, however, the formation of adhesions goes on less obtrusively, often entirely latently; whence the symptoms that develop later are commonly misinterpreted. In consequence of milder infections the less virulent toxins give rise to less desquamation of peritoneal endothelium, to the exudation of less fibrinous lymph, and to less inflammatory phenomena—sufficient, however, often to lead to more or less widespread adhesions. Frequently, these are quite localized and very delicate (gall-spiders, resembling spider-webs, they have been aptly called by Morris); in other cases they are widespread and very dense.

All gradations are encountered, from those so delicate and slight as scarcely to occasion comment or awaken interest, and possibly, though certainly not always, innocuous clinically, to others so dense and unyielding that the wonder is that the patient has been able so long to withstand their effects. Of the 216 patients in Kelly's list 123 had adhesions, 22 had no adhesions, and in 71 the presence or absence of adhesions is not mentioned (probably none were present).

The clinical recognition of these adhesions is sometimes a matter of difficulty, but is perhaps not impossible in the majority of cases. It is essential, in the first place, that we recognize that many of the cases of so-called "stomach ache," "biliousness," indigestion, gastralgia, gastritis, gastroduodenitis, persistent or recurring vomiting, constipation, etc., in reality have an anatomical basis. We now know that many of these cases are due to an unsuspected or latent gastric or duodenal ulcer, definite cholecystitis, chronic pancreatitis, etc.; in other cases they are due to pericholecystic, perigastric, periduodenal, and pericolonic adhesions. We must study attentively patients who complain of general ill-health, with more or less ill-defined gastric or epigastric symptoms, epigastric distress and tenderness, sometimes associated with nausea and vomiting, and perhaps constipation. Attacks of such symptoms

may come on periodically without definite cause: they may last a few days, and cease quite as causelessly. Now and then the attacks may be ushered in with chilliness (rarely a definite chill), and may be attended by a little fever.

Examination may reveal some tenderness in the epigastrium, perhaps a little to the right of the median line, toward the region of the pylorus or gall-bladder, and some rigidity of the overlying muscle. Deep pressure is sometimes very painful. Later, the pylorus or the duodenum may become obstructed, the commoner manifestations of dilatation of the stomach supervene; in such cases especial diagnostic importance attaches to intractability of the symptoms and a history of past infection of the biliary tract (typhoid fever, cholecystitis, cholangitis, jaundice, etc.). In the event of suspecting such adhesions, we must exclude other factors that may cause similar symptoms, remembering, however, that in many cases symptoms supposedly due to disease of the stomach or intestine are due to disease of the gall-bladder or adhesions of the upper abdomen.

*The General Principles of the Medical Treatment of Gallstones.* Because we have not understood the pathology of the biliary system in the past, it has been impossible to formulate a rational or satisfactory means of medical treatment. The surgeons have made better progress in this direction than the internists, and among the more progressive part of the profession it has become the tendency in recent times to consider surgery the only means of relief. The more recent developments of our knowledge of the morbid physiology of the biliary system has shown us that while medical treatment has its limitations it can accomplish much, even enough in many cases to make surgery unnecessary. In no condition more than in gallstone disease is a knowledge of the natural history of the affection more necessary for its intelligent treatment. We must recognize our limitations and must not attempt to dissolve by medical means a stone that is insoluble; to cause the passage through the gall-ducts of a gallstone when the ducts are impassable to a stone of its size; to attempt to cure supposed gastric symptoms by measures directed to the stomach when the cause of the symptoms is adhesions about the gall-bladder, and to cause the solution of these adhesions in case they have been diagnosticated. Yet medical treatment has come to have a very definite place in biliary affection and has been placed upon a rational basis. The main indications as given by Kelly are:

*Solution of the Gallstones.* As regards the solubility of the gallstones, Naunyn states that we have to consider cholesterin, bilirubin-calcium, calcium carbonate, and calcium phosphate. Of these, bilirubin-calcium and the inorganic salts of calcium are insoluble in the bile; cholesterin, however, is quite soluble in the bile, and even in conditions of disease the bile scarcely if ever contains so much cholesterin that it cannot take more in solution. We have, therefore, to admit the



possibility of cholesterin stones being dissolved. In fact, there is some experimental evidence that goes to prove that not only in vitro, but also in vivo, cholesterin stones may be dissolved. Naunyn quotes Labes' experiments of thirty years ago, in which he introduced gallstones into the gall-bladder of dogs and, killing the animals two months later, found that partial solution of the stones had occurred. Recently, Bain<sup>1</sup> has published the results of some studies that show the same possibility. In these experiments, however, the calculi were introduced into normal gall-bladders (or, as in one or two of Bain's experiments, into gall-bladders in which a cholecystitis has been artificially produced). The conditions are quite different in the human subject affected with gallstones, in which we have to deal not only with the stones as such, but also with the subacute or chronic catarrh, the direct cause of the gallstone formation. It is thus exceedingly doubtful whether spontaneous solution of gallstones ever occurs in the human subject; indeed, whether it is at all possible. Naunyn states that in studying one thousand cases of cholelithiasis he has seen trustworthy evidence of the solution of the stone in perhaps ten cases (1 per cent.). The reasons for the non-occurrence of solution of the stones are (1) that on account of the presence of the stones the activity of the walls of the gall-bladder is compromised; it cannot empty itself completely (a certain amount of residual bile is always present), and the desirable irrigation of the gall-bladder with fresh bile (the solvent menstruum) does not occur; and (2) that on account of the associated catarrh of the biliary tract the bile contains more cholesterin than is normal, and thus takes up an additional increased amount with less avidity.

Naunyn furthermore points out that even should it be possible to cause disintegration of the stones in the gall-bladder, it is exceedingly doubtful how much good would be thereby accomplished, since in this event the residual particles of the disintegrated calculi would remain in the gall-bladder and form the neucles of new calculi. These are formed by the cementing together or incrustation of the disintegrated particles by newly precipitated bilirubin-calcium, the formation of which is favored by the persisting infectious inflammation of the mucous membrane which gives rise to a secretion rich in calcium.

This reasoning is well borne out by clinical experience, since it is exceedingly doubtful whether, with any means at our command, we can cause solution of gallstones in the gall-bladder. We now know that thousands of gallstones said to have been passed by the bowel after the administration of olive oil are merely masses resembling gallstones in outward appearances and due to deceptive changes in the olive oil acquired in its passage through the intestinal tract. We must conclude, then, that the solution of gallstones is scarcely the object of rational treatment.

<sup>1</sup> PROGRESSIVE MEDICINE, December 1906.

*Discharge of Gallstones.* They may be discharged from the biliary tract by way of the ducts or by fistula. Many stones rarely pass out through the ducts, though single stones sometimes do; large stones, particularly if they leave the gall-bladder at all, escape by the formation of fistulae. In some cases the gallstones have been entirely latent until they appear in the stools, in which event if the stone is large we must assume the formation of a gall-bladder-colonic fistula, since large stones having ulcerated into the small intestine practically always cause noteworthy symptoms in their downward passage, and not infrequently even fatal intestinal obstruction. In the event of a single stone only being present, the possibility of cure is thus presented, but the possibility is too remote for serious consideration. It is an occurrence which should not be hoped for, nor awaited, nor sought by medical means, even were such at our command; it also then cannot be considered an object of rational treatment.

*Treatment of the Infection.* It will be seen that the aims of medical treatment should not be directed toward the solution of the stones, nor toward effecting their discharge through the ducts. The great hope in medical treatment is to restore the latency of the condition by treating the infection and through influencing it to render the mucous membrane of the biliary system approximately healthy. Unquestionably medical treatment can accomplish much in this direction and can often effect a virtual cure, but the physician must recognize his limitations and must not subject his patient too long to a useless medicinal treatment when early surgical interference may restore him to health and delay in operation may be actually dangerous. By promoting the free flow of bile we may effect the discharge of the infective bacteria and their toxin from the biliary tract and prevent their ascent into the smaller ducts. Ultimately the tract may be rendered sterile and should the inflammation eventually subside a condition of latency and quiescence results. In rare cases this is permanent. In most cases, however, a low grade of catarrh of the gall-bladder persists, and it becomes a point of lesser resistance which readily becomes infected and the patient consequently is continuously or intermittently ill. Should gallstones be passed by the bowel, we must remember that all the gallstones harbored by the patient are seldom, if ever, thus passed, and even were this the case the persisting catarrh of the gall-bladder is quite certain to give rise to the formation of new stones.

*Indications for Surgical Intervention.* The object of surgical interference is of course to remove the stones, but to my mind the next important thing to be accomplished by the surgeon is to drain the biliary system and through it the pancreatic ducts. By this means the infection is relieved, the mucous membrane returns to a healthy condition, and the danger of further formation of stones and chronic pancreatitis is removed. In discussing the best time for operation Kelly says that

in many cases the question of early operation scarcely admits of discussion. These are cases in which there is acute cholecystitis (with or without cholangitis and jaundice), with evidence of severe infection, and in which the symptoms and local signs, instead of abating, become more pronounced; these comprise cases of acute cholecystitis developing during or after an attack of typhoid fever or other infectious disease, as well as during the course of previously latent or manifest cholelithiasis; cases in which the diagnosis of severe suppurative or gangrenous cholecystitis with perforation of the gall-bladder or severe local or generalized peritonitis seems warranted, and in which impending if not actual infection of the hepatic ducts is not unlikely. The risk attending the progress of the disease in such cases is more than the hazard of the operation; indeed, without operation many of these cases would unquestionably soon terminate fatally. Happily, however, most of the acute infections of the biliary tract subside spontaneously, or, under the beneficent influence of wisely directed medicinal treatment, even many of those that develop very suddenly and in which the outlook during the first twelve or twenty-four hours seems fraught with danger. In general it is much wiser that the acute manifestations should subside without operation, which, should it be deemed desirable later, with a view to relieve the basic condition, may then be undertaken with much more reasonable hope of ultimate success. Immediate operation is also imperative in the event of acute intestinal obstruction in a case of gallstones, or in a person in whom adhesions have been suspected. Operation, though not necessarily always immediate, is indicated in all cases of persistently enlarged gall-bladder, whether the enlargement is due to simple hydrops (serous and mucous fluid), empyema (pus), or gallstones.

The question of when to operate in cases of gallstones that have become or have been active must be decided in each individual case; but one should bear in mind that, as a rule, it is not the many stones in the gall-bladder that do the most damage, but the one or two stones that get into the ducts; that the special risk attending operations for gallstones increases with delay, and that, whereas gallstones are readily removed from the gall-bladder, their removal from the ducts is commonly attended by serious difficulties and is sometimes impossible. The time of election for operation, therefore, is before the stones have entered the ducts. This is by no means always possible, nor indeed desirable. Thus, I should not advise the removal of stones that are and always have been quiescent. If, however, the gall-bladder is enlarged, and the stones have given warnings of discontent with their hampered quarters, local discomfort and distress, operation should be undertaken. Kelly does not insist upon operation after a single short gallstone colic, for some patients have only a single attack. However, most patients have many attacks and in Kelly's experience two or three attacks is a positive indication for operation.

In impaction of a gallstone with chronic jaundice operation is called for, and this should be early rather than delayed. The risk of gallstone operations is the risk of delay, since with delay serious infections of the biliary tract may supervene (with the characteristic intermittent fever, etc.), the tendency to pronounced hemorrhage increases with the persistence of the jaundice, the general nutrition of the patient fails, and he becomes less able to withstand the vicissitudes of the operation, and stagnation of bile leads to dilatation of the ducts, compromising the functional activity of the liver cells.

Finally, operation is indicated in those obscure cases usually diagnosed indigestion, biliousness, gastralgia, recurring vomiting, etc., in which with reasonable certainty the presence of pericystic, perigastric, or periduodenal adhesions may be surmised.

In each of the foregoing classes of cases, and in which the patient's ailment is persistent and serious enough to want surgical intervention, operative intervention attains that which is impossible of attainment, or attainable only with difficulty with medicinal measures. Surgery finds additional justification in the fact that early intervention tends to prevent the development of certain complications and sequels, such as extensive adhesions, fistulæ, carcinoma of the gall-bladder, acute and chronic pancreatitis, etc. An operation, however, should not be lightly undertaken in persons suffering with certain disorders of nutrition, such as gout, obesity, so-called chronic rheumatism, or diabetes; nor in those with faulty kidneys, lungs, or heart. In such cases the risk attending the anesthesia and the shock of the operation is too great and the recuperative power of the patient too much reduced to expect from operation a great deal more than can probably be attained by well-directed medicinal, hygienic, and dietetic treatment. Finally, the fact that operative results are not always what are hoped for is not in itself a contra-indication to operation; on the contrary, these untoward results are often attributable rather to the fact that in many long-delayed cases the anatomical lesions are such as to be almost, if not quite, irremediable by any and all means at our command.

It will be seen from Kelly's paper, which is very complete and well considered, that the treatment for biliary infection is really surgical. If, however, there are contra-indications against operation either because of the patient's opposition or his physical condition, then much can be hoped from medicinal treatment in favorable cases. Indeed in some instances a virtual cure can be accomplished.

**Chronic Icterus.** Within recent years there have been about 30 cases of chronic icterus reported which cannot be classified under any of our hitherto recognized diseases; 2 cases reported by Claus and Kalberlah<sup>1</sup> will serve as examples.

These cases were two brothers with chronic jaundice, and among

<sup>1</sup> Berl klin. Wochenschrift, 1906, xliii, Nr. 46, 1471.

whose maternal relatives chronic icterus and decided splenic enlargement had occurred. The older brother, aged twenty-six years at the time of observation, had had pleurisy in childhood, succeeded by the development of icterus with splenic tumor, enlargement of the liver, and anemia. The younger brother developed during his military service a moderate jaundice, following an insignificant digestive disturbance. The stools were colored in both cases. In the older brother's case the urine at first contained bilirubin, which later disappeared; the urine of the younger brother never contained biliary coloring matter.

In reviewing the 29 reported cases it is observed that splenic tumor was present in 21. The blood findings were practically normal. Enlargement of the liver was reported in 14 cases. The urine usually contained urobilin, but even this was absent in some cases; 1 case exhibited bilirubin occasionally. In 14 cases the jaundice was positively congenital, in 5 cases probably congenital, and in 10 cases acquired after birth. The presence of splenic tumor and absence of hepatic enlargement are considered as somewhat characteristic of the congenital cases, while a large liver is almost invariably present in the acquired cases.

When it comes to the question of etiology, each author has a different opinion. Minkowski regards the affection as an anomaly in the metabolism of the blood pigment, perhaps a result of primary changes in the spleen. Kranhals also regards the splenic tumor as the primary condition, but assumes that the destruction of the red corpuscles is due to the action of a toxin on the liver.

A. Pick, in whose cases both hepatic and splenic enlargement was wanting, believes that there is a congenital communication between the lymph channels and the bile passages. Widal and Ravant believe that in their cases there was a congenital degenerative condition of the liver, with overproduction of bile. The French authors, most of whose cases were of the acquired variety, assume a chronic infection of the biliary passages as the etiological factor, favored by a hereditary biliary diathesis. The 2 cases here reported by Claus and Kalberlah seem to belong to this last category. The coloration of the stools would point to an overproduction of bile, with which is connected the increased disintegration of the red corpuscles. The indications, therefore, are that the primary cause of the affection lies in the liver. The overproduction of bile, together with a possible injury of the hepatic cells, leads to a diffusion of the bile into the lymph channels and bloodvessels. The splenic tumor will then have to be regarded as a secondary phenomenon.

In view of this diversity of opinion, it is probably safe to assume that the cases are not all due to the same cause. A review of the 29 cases gives the impression that there are two fundamental classes: the congenital cases with primary changes in the spleen and the acquired cases with primary changes in the liver. The future nomenclature of these cases of chronic icterus should take into consideration these fundamental differences.

**ACQUIRED FORMS OF CHRONIC ACHOLURIC ICTERUS WITH SPLENO-MEGALY.** H. Strauss<sup>1</sup> reports 2 cases belonging to the class designated acquired, as distinguished from the congenital cases. Both patients were in the third decade of life, one having been jaundiced for twenty-three years and the other for an indefinite number of years. The stools in both cases had always been brown, and the urine yellow or reddish. There was also a marked swelling of the spleen, a slight enlargement of the liver, and the absence of bilirubin, but presence of urobilin in the urine. There was also a tendency to gastro-intestinal disturbances—constipation, pressure in the gastric and hepatic region, a certain amount of general weakness, and in one case a tendency to occasional diarrhea. Both patients were subject to repeated attacks of pain in the upper abdomen and one of them had occasional chills. No history or evidence of syphilis, cholelithiasis, echinococcus disease, leukemia, pseudoleukemia, or malaria could be elicited.

**The Causes of the Increased Portal Pressure in Portal Cirrhosis.** Ever since we have known anything of the anatomical changes in the liver in cirrhosis, it has been assumed that the portal obstruction, which is such a prominent symptom of the disease, was due to constriction of the radicles of the portal vein by the surrounding new-formed connective tissue.

The experimental work of Frederick C. Herrick<sup>2</sup> has put an entirely new light upon the matter. He shows that the portal veins are rather more patulous and pervious to fluids in cirrhosis than in health, and that the rise in the portal pressure and the resulting obstruction are due not to the compression of the veins, but to an increased arterial flow. If Herrick's work is verified, it will prove to be one of the most notable advances in our knowledge of the morbid physiology of the liver that has been made in recent times. The methods of investigation employed by Herrick were as follows:

For normal livers only those were used which were free from possible disease. No livers altered by passive congestion were used; only typical cirrhotic livers were used for that part of the research which concerns this condition. Microscopic sections were made of each liver and the condition verified. The livers were taken never longer than twenty-four hours post-mortem and were never kept longer than twenty-four hours after being removed from the body. When they were kept overnight it was always in normal saline in cold storage. Comparisons of the two circulations in the same liver only were made. The two circulations in different livers were not compared. The circulating fluids used were normal saline solutions at 38° to 39° C. At the end of the experiments he used defibrinated sheep's blood fresh from the animals for verification. The livers were always immersed in their natural position in normal saline at body tem-

<sup>1</sup> Berl. klin. Wochenschrift, 1906, xliii, Nr 50, 1590.

<sup>2</sup> Journal of Experimental Medicine, January, 1907. From the Rockefeller Institute

perature. Mercury manometers were used to measure pressures. In every case the liver was washed of blood at the normal pressure of 130 mm. for the arterial and 10 mm. for the portal vessels. They were next washed backward by a pressure of 10 to 20 mm. through the hepatic veins. It required from ten to fifteen minutes to wash a liver preparatory to the experiments. Bits of washed fibrin were occasionally floated out and especially backward from the hepatic to the portal vein. The first estimations were always made on both circulations together at normal pressures. These were then varied within the limits of from zero to 140 mm. arterial and zero to 20 mm. portal pressure. The pressures were always put on together, and variations made as nearly as possible in the normal ratio. The portal circulation was next studied alone at variable pressures. The arterial was then considered alone with its higher pressures. By this order an unnatural dilatation of the vessels was prevented.

After the experiments the livers were sliced into sections 1 cm. thick and the macroscopic vessels examined for possible occluding fibrin. In but 1 case was fibrin found in a portal vessel of importance, a vein of about 3 mm. diameter. Sections for histological study were then made.

His conclusions were as follows:

1. In the liver of portal cirrhosis there is a far freer communication between the arterial and portal currents than in the normal liver.

2. The factors contributing to the increased portal pressure in cirrhosis are: this direct communication of the arterial pressure to the portal vessels through dilated capillaries combined with the larger volume flow of the hepatic artery in cirrhosis as compared to that in the normal liver.

3. A portal cirrhotic liver gives passage to an amount of portal fluid proportionate to its weight. There is no obstruction to the portal vessels from fibrous tissue around them.

4. The communication of the arterial pressure is an important factor in explaining the increased portal pressure. Put into other words this means that the portal pressure is increased in portal cirrhosis because the arterial flow is increased. This takes place because a larger arterial supply is demanded by the recently formed and growing connective tissue. This affects the portal circulation because there is a very free communication between the arterial and portal circulation—freer in cirrhosis than in health, because in cirrhosis there are more capillaries; consequently, the rise in arterial pressure causes a rise in portal pressure. This is much more liable to occur if there is at the same time a retardation of the venous flow from myocardial weakness, as there is apt to be in cirrhosis.

Herrick's investigation showed several other points, namely: (1) From an arterial inflow there is a free return flow through the portal as well as through the hepatic veins in both normal and cirrhotic livers. (2) From a portal inflow the return is through the hepatic vein only. Gad's theory that the entrance from the arterioles into the veins are guarded by valves which allow the blood to flow only in one direction and prevents regurgitation is the most reasonable explanation of this phenomenon,

Clinically the investigations of Herrick will make no immediate difference in our earlier ideas of the symptomatology or treatment of cirrhosis. Pathologically it alters our conceptions of the cause of portal obstruction and is a very interesting and important communication.

### THE PANCREAS.

**Pathogenesis of Acute Hemorrhage and Necrosis of the Pancreas.** The numerous experiments intended to determine the pathogenesis of acute pancreatic disease with fat necrosis have as yet not been entirely satisfactory. Simple ligation of the pancreatic bloodvessels does not produce fat necrosis, while Opie's experiment, of injecting bile into the pancreatic duct, apparently does not cover all cases. The autodigestion theory, as heretofore promulgated, leaves out of consideration the demonstrated fact that native pancreatic secretion has no power of digesting proteids. The inefficient trypsinogen of pancreatic juice is converted into active trypsin only by the addition of enterokinase, obtained from the mucous membrane of the duodenum and upper jejunum. It has, therefore, occurred to E. A. Pólya<sup>1</sup> that a mixture of intestinal secretion with pancreatic juice within the pancreas itself produces autolysis of the pancreatic epithelium and connective tissue, and that the digestive juices thus reach the peripancreatic fat, to produce necrosis of the same.

In order to support this theory, Pólya carried out a series of experiments in lower animals. Extracts of intestinal mucous membrane were injected into the pancreatic tissue and into the pancreatic duct of various animals. In two-thirds of the cases death ensued within twenty-four hours, autopsies showing necrosis and hemorrhage of the pancreas, with more or less extensive fat necrosis. Most of the animals that survived showed for a time severe symptoms.

The negative results can be explained either by faulty technique or by natural resistance of the animal. Where the experiment was made with intestinal contents, it was invariably successful in producing fatal pancreatic lesions. The same results were obtained by the injection of trypsin solutions into the pancreatic duct. The most positive results were obtained by the injection of duodenal contents into the pancreatic duct. It has been shown by previous experiments that this effect of the duodenal contents can be due neither to the contained bacteria nor to the small quantities of oil, blood, hydrochloric acid, bile, fatty acids, etc., present in the duodenum. Hence, it is fair to deduce that the pancreatic lesions and fat necrosis are due to the action of trypsin, which is formed by the introduction of intestinal secretion into the pancreas by way of its excretory duct. The demonstration of how the intestinal juice gains access to the pancreas in the human body remains for future investigation.

<sup>1</sup> Berl. klin. Wochenschrift, 1906, xliii, Nr. 49, 1562.



# DISEASES OF THE KIDNEYS.

By JOHN ROSE BRADFORD, M.D.

**Pathology of Hydronephrosis.** Hydronephrosis is dependent on the retention of urine in the pelvis of the kidney which secondarily undergoes a dilatation to a greater or less degree, and thus is always dependent on an obstacle to the free exit of urine. Hydronephrosis may be classified into two groups: the one of congenital origin, the other where the obstruction is due to some acquired cause. Some writers have restricted the term congenital hydronephrosis to the form of the disease not only due to a congenital malformation, but appearing only in the first two years of life. Albarran<sup>1</sup> and most authors consider that the term congenital should be employed wherever there is a malformation, notwithstanding the fact that the hydronephrosis does not appear until adult life or even later.

In the course of embryonic development the ureter undergoes rotation amounting to 180 degrees round the Wolffian duct, and thus a whole series of malformations may result in the course of erroneous development.

An obstruction to the exit of urine may be developed either in the inferior or superior portion of the ureter, and in some cases malformations of the kidney may secondarily give rise to obstruction of the ureter and thus lead to the development of hydronephrosis.

Congenital anomalies even of the urethra, especially the presence of valvular folds in the mucous membrane, may give rise to hydronephrosis, but in this variety of the disease the ureters in their whole length and the urinary bladder are also greatly dilated.

Even in cases of extroverted bladder hydronephrosis may develop and this, according to Albarran, is not to be looked upon as a result of the ascending infection that is so frequently present in these cases, but this ascending infection is rather to be regarded as liable to develop to an undue extent owing to the hydronephrosis and dilatation of the ureters produced as a result of the extroversion of the bladder. He considers that the terminal portion of the ureters are liable to be compressed by the intestine, inasmuch as the posterior wall of the bladder forms the covering of a hernia and at its neck the ureters are more or less compressed.

*Congenital hydronephrosis* dependent on malformation of the ureters may be divided into three classes: those due to anomalies in the number of the ureters, anomalies of position, and anomalies of caliber.

<sup>1</sup> Annales des maladies des organes génitourinaires, 1907, vol. i, Nos. 11 and 12; vol. ii, No. 13

Want of development of the ureter, provided the renal pelvis is present, may give rise to the development of hydronephrosis, but such cases are very rare.

Anomalous positions of the ureter may be dependent on an abnormal opening of the ureter into the bladder or else on congenital kinking or on the ureter being compressed by bands.

The ureter may open in many abnormal positions; thus, in rare instances it may open into the intestine by a narrow orifice or in some cases the connection may be a blind one. In some instances the ureter descends to the lower part of the bladder and then rises in an oblique manner to open into the trigone. In this way sufficient obstruction can be produced to cause hydronephrosis. Or else the ureter may reach the bladder high up on its posterior surface and run an oblique course on the wall of the bladder before opening into the trigone.

A more common abnormality is for the ureter to open into the prostatic portion of the urethra, and in these circumstances the communication may be a very narrow one and lead to great obstruction. In the female the ureter may open into the urethra or more rarely into the vagina or even into the vestibule.

In those cases where the ureter opens abnormally a double ureter may also be present, and the hydronephrosis may only involve one ureter and the portion of kidney attached to it. According to Albarran, whenever a double ureter is associated with hydronephrosis it is always the upper portion of the kidney that becomes hydronephrotic.

Congenital kinking may be dependent on an abnormal situation of the kidney or else be brought about as a result of obstruction produced by bloodvessels or by bands. When the position of the kidney is abnormal hydronephrosis may result, whether the kidney be fixed or whether it is mobile. In some very rare instances hydronephrosis has resulted where but a single kidney is present, and a number of cases have been described where hydronephrosis associated with a horseshoe kidney coexisted. Albarran does not consider that the mere presence of an abnormal artery, whether it passes in front or behind the ureter, is of itself a sufficient cause for the production of hydronephrosis, but if the kidney at the same time undergoes displacement and descends, then it is obvious that the ureter may become kinked over the vessel. Thus it is probable that where hydronephrosis has been attributed to the presence of abnormal vessels the kidney was really mobile in addition.

Finally in rare instances bands have been found around the ureter and compressing it, and it has been thought that these bands may be relics of the Wolffian or Müllerian duct.

Diminution in the caliber of the ureter may be of congenital origin and be the result of the presence of valvular folds of the mucous membrane or on the ureter being imperforate. In the fetus of three or four months the mucous membrane in the ureter shows numerous longitudinal

and transverse folds of the mucous membrane. Later on in fetal life these folds disappear, but their persistence may give rise to obstruction.

Further, the ureter may be narrowed congenitally either at its junction with the renal pelvis or with the bladder, and this variety of urethral obstruction is looked upon by many as a frequent cause of hydronephrosis in adults.

*Acquired hydronephrosis*, like the congenital variety, is also dependent on an obstacle to the exit of the urine, and this may be present in the urethra, bladder, ureter, or renal pelvis. Retention of urine in the bladder may lead to the development of hydronephrosis, but this is not usually dependent on any reflux from the urine in the bladder into the ureter, but rather on the obstacle to the free exit of urine from the ureter into the bladder. The distention of the bladder leads to some compression of the ureter on its way to the trigone and in some instances of cystitis the hypertrophy of the vesical mucous membrane surrounding the orifice of the ureter may lead to its obstruction. It is only in comparatively rare instances that the vesical orifice of the ureter becomes dilated and patent. In most cases where the obstruction is of vesical origin only the dilatation of the ureter and of the renal pelvis results and true hydronephrosis does not develop. In a large number of cases of hydronephrosis in adults the ureter is found attached to the middle or upper part of the dilated renal pelvis so that there is a pouch below the attachment of the ureter. Very often the attachment of the ureter is oblique and not uncommonly a valvular orifice is thus produced and, further, a kinking of the ureter in this position may be observed. These conditions have often been regarded as causes of the hydronephrosis, but Albarran points out very conclusively that they are rather to be looked upon as the results rather than the causes. It is possible that in some instances the abnormal position of the ureters may be of congenital origin or else it may be that hydronephrosis has been produced by some other cause which has disappeared at the time the examination was made and only the results of the hydronephrosis are observed. Albarran draws attention to the fact that a high attachment of the ureter to the renal pelvis is not observed as a congenital lesion, and thus it is difficult to regard it as a cause of hydronephrosis. Further, in young children renal lithiasis is not uncommon and small calculi are not unfrequently observed. Thus a calculus may have given rise to hydronephrosis and the subsequent dilatation or the consequent dilatation of the renal pelvis may be the cause of the apparent anomalous connection of the ureter.

Experimental ligation of the ureter in animals followed by the development of hydronephrosis gives rise to very similar anatomical changes to those just described.

It is possible that in some instances the structure of the renal pelvis may predispose to hydronephrosis and some writers have considered want of development of the muscular tissue of the renal pelvis as a pos-

sible cause. Albarran considers that the oblique insertion of the ureter, the valvular forms of the mucous membrane, and even the kinking of the ureter so often looked upon as causes of hydronephrosis are very frequently the results brought about by hydronephrosis dependent on other causes.

The most interesting form of kinking of the ureter is that associated with *movable kidney*. So frequently are these two conditions associated that the occurrence of a hydronephrosis in cases of movable kidney has been looked upon as conclusive proof that the hydronephrosis is actually produced by the kink. The fact that hydronephrosis in these cases is very often intermittent has also been regarded as further evidence in support of this view, but Albarran holds strongly that the increased flow of urine so often seen coincidently with the subsidence of the hydronephrosis is not really dependent on the emptying of the hydronephrotic sac. He states that he has often observed, when operating on patients during the period of renal enlargement, that the increase in the size of the kidney is not dependent on distention of the renal pelvis, but really due to very great congestion of the organ; and, further, that he has observed cases where, during the *crise d'hydronephrose* the kidney was small and yet the subsidence of the attack was associated with the passage of one liter to one liter and a half of urine. He also states that he has shown, by catheterization of the ureter and the evacuation of a small hydronephrotic collection of urine, that such patients have subsequently passed a very large quantity of urine. Intermittence is observed in all varieties of hydronephrosis and, among others, where the condition is due to calculous obstruction or even to that produced by neoplasms. He evidently regards the polyuria as dependent on some reflex agency acting on the other kidney, and concludes that intermittent hydronephrosis cannot be looked upon as dependent merely upon kinking of the ureter.

The fixation of the kidney is often followed by disappearance of the hydronephrosis. In some instances the kinked ureter is obstructed owing to the formation of adhesions between it and the surrounding structures, leading to varying degrees in the diminution of its caliber, and in operations for the relief of hydronephrosis it is desirable to look for these and to free them. Albarran considers that in many cases of movable kidney the kinking of the ureter and even the formation of adhesions obstructing its lumen are consequences of the hydronephrosis, inflammatory processes arising secondarily as a result of the dilatation of the ureter.

In rare instances kinks may be present in the ureter in the lower part of its course, and may be brought about as a result of inflammatory affections in its vicinity. Prolapse of the uterus may give rise to hydronephrosis from kinking of the ureter.

Acquired hydronephrosis necessarily often follows compression of the ureter, and this is much more common in women than in men. Albar-

ran draws attention to the occurrence of hydronephrosis in association with pregnancy, and points out that a hydronephrosis arising in this way may persist and even increase in amount long after the pregnancy. In man pericystitis and periprostatitis may sometimes lead to obstruction of the ureter, but these are rare causes when compared with malignant growths in the pelvis, bladder, and prostate.

Hydronephrosis sometimes results from narrowing of the ureter as a sequel to a lesion of its walls produced by traumatism, inflammation of the ureter, or the presence of new-growths. Traumatic hydronephrosis dependent on lesion of the ureter is uncommon, and many of the cases regarded as such are really cases where the urine is extravasated, forming a perinephritic collection, but in some instances of rupture of the ureter acute hydronephrosis develops.

Hydronephrosis sometimes follows operations and more especially operations on the pelvic organs, but in some instances it has been known to follow the operation of fixing the kidney where this organ is mobile, but where prior to the operation no hydronephrosis was present.

Stricture of the ureter as the result of inflammation of the mucous membrane is one of the rarer causes of hydronephrosis and such ureteritis may be an ascending one or more rarely descending. In some instances a stricture may be brought about as the result of an ulcer produced by a calculus.

New-growths, both simple and malignant, papillomas and adenomas, may arise in the ureter and lead to its obstruction.

Hydronephrosis as the result of calculous obstruction is of course very common and Albarran considers that the fact that it does not always occur depends on the degree of obstruction produced by the calculus and also on the state of the kidney. He agrees that experimentally complete obstruction of the ureter is invariably followed by the development of hydronephrosis, and that Cohnheim's theory that hydronephrosis only resulted where the obstruction was partial and that suppression occurred where the obstruction was complete is probably erroneous. Hence, if the calculous obstruction takes place in an individual where the kidney is healthy hydronephrosis will develop; on the other hand, if the kidney is diseased and especially if the renal pelvis is thickened it is possible that it may not occur. The complete suppression not uncommonly seen as a result of calculous obstruction may in some instances be due to reflex suppression, but unquestionably it is most often dependent on the fact that the ureter of the only available kidney is obstructed.

Albarran concludes his article by drawing attention to the important practical point that the presence in the upper part of the ureter or of the renal pelvis of certain lesions, such as kinking of the ureter or the attachment of the ureter higher than normal, may be really secondary lesions dependent on hydronephrosis produced by a cause acting on the lower part of the ureter. In all operations for the relief of hydronephrosis it is,

therefore, essential not to confine the examination to the upper part of the ureter, but to explore the caliber of this channel throughout its length, as otherwise lesions in the upper, which are really the result of the hydro-nephrosis, may be looked upon as its cause.

**Renal Tumors in Children.** **ETIOLOGY.** Renal tumors are a little less frequent in childhood than in the adult, and but 173 cases are recorded in contrast to the 416 in adults. It is of some interest that up to the age of sixteen malignant disease tends to affect especially the kidney, since according to Mouchet<sup>1</sup> from 45 to 50 per cent. of all cases of malignant disease in childhood involve the kidneys. Further, renal tumors develop especially during the first three years of life, and 75 per cent. of the malignant neoplasms of the kidney in childhood appear before the age of four, and in a considerable proportion of cases these tumors develop within the first year of life. They may be present at birth and they have been observed to develop during intra-uterine life, in one case in a fetus of seven months. These tumors are rather more frequent in boys than in girls. In 4 cases among 137 observations the tumor was bilateral, but it is difficult to distinguish cases of true bilaterality from those in which the second kidney is involved as a result of metastatic deposits.

**PATHOLOGY.** Mouchet draws attention to the great differences of opinion that have been held with regard to the nature of renal tumors. Formerly malignant renal tumors in the young were looked upon as sarcomatous and those in adults as carcinomatous. Subsequently to this renal tumors were classified according as to their supposed mode of development from normal constituents of the kidney; thus, some were regarded as developed from the epithelium of the uriniferous tubules and others from the connective tissue. At a later period Grawitz in 1883 called attention to the part played by suprarenal rests in the development of renal tumors, and these tumors received the name of *hypernephromas*.

More recently renal tumors have been divided into epitheliomas, sarcomas, including the true sarcomas; the angiosarcoma, the endothelioma, and a mixed tumor containing various tissue elements, some resembling epithelial structures and others connective tissue. Some writers have thought that the greater number of renal tumors were hypernephromas, and Albrecht considered that 69 out of 103 tumors of the kidney fell into this category. These hypernephromas vary a good deal in their structure; in some instances the adenomatous element is the more developed, and thus the growth presents considerable resemblance to a true carcinoma, whereas in others connective-tissue elements are the more developed and thus a resemblance to a sarcoma is produced.

Mouchet considers that if renal tumors be divided into epitheliomas, sarcomas, and mixed tumors, the true sarcomas are rare; that the great bulk of renal tumors fall into the third category of mixed tumors, and

<sup>1</sup> Annales des maladies des organes génitourinaires, March, 1907, vol. i, No. 5.

that in the case of children almost all the renal tumors belong to this group. From a histological point of view these tumors have a complex structure. Thus they have a stroma resembling embryonic connective tissue which presents many points of similarity with sarcoma, but masses of cartilage, of muscular tissue, both striated and unstriated, and, finally, epithelial elements arranged in alveoli are also present. According to him the structure of these neoplasms is never simple, and even if the sarcomatous element preponderate, muscular fibers, both striated and unstriated, and epithelial elements, etc., are always to be found. As Mouchet points out, it is difficult to believe that tumors of this complex structure can arise from any normal element of the kidney, since it is difficult to explain on this theory the presence of striped muscular fiber.

It is equally difficult to account for the origin of these tumors in suprarenal rests, and Mouchet thinks the presence of these different tissue elements, together with the extraordinary frequency with which these tumors occur in the earlier years, is conclusive evidence in favor of their congenital origin, and he is in favor of Wilms' theory that these tumors are the result of mesenchyme inclusions in the early stages of development. The striated muscular fibers present in the tumor would then arise from a myotome and the islets of cartilage from the embryonic tissue destined to the formation of the vertebral column, and the glandular structures present in the tumor would arise either from the cell elements destined to form the kidney or from those giving rise to the mesonephros. Thus the mixed tumor of the kidney may be due either to the inclusion of the myotome, of the sclerotome, or of the mesonephros. If this view be accepted the renal tumors would present many points of similarity in their origin with the mixed tumors of the parotid or those of the testicle.

There is some evidence that the left kidney may be involved somewhat more frequently than the right, and it is possible that the lower extremity of the organ may be involved before the upper. In some instances of rapid growth the tumor may escape from the capsule of the kidney, and where the tumor reaches a very large size scarcely any trace of the kidney can be found. In children the peritoneum is apt to be involved early, but according to Mouchet, although secondary glandular deposits usually occur, they tend to occur late; the generalization of the disease takes place usually *via* the lymphatics, but in some cases also by means of the venous system, and extensive thrombosis of the vena cava may take place. Embolism from the detachment of portions of the malignant growth in the interior of the vein are not uncommon and the lung is necessarily the organ most frequently involved.

**SYMPTOMS.** The presence of a tumor, hematuria, and pain are, of course, the classical phenomena seen in malignant disease of the kidney, but in the case of children the presence of the tumor is by far the most important fact and is very often the initial manifestation of the disease, and generally the predominant effect produced until the later stages, when

cachexia appears. Patients do not usually come under observation until the tumor has reached such a size as to cause enlargement of the abdomen. The veins of the abdominal wall are often notably enlarged, but varicocele would appear to be rare as compared with its frequency in adults. The presence of a renal tumor has usually to be determined by palpation; percussion is of but little importance in the case of children.

Hematuria would appear to be rather uncommon in children affected with malignant disease as compared with its frequency in adults, and was only noted in some 16 out of 100 cases. The hematuria is characterized by the fact that the blood is uniformly diffused in the urine and that the attack is spontaneous, occurring apparently without cause and often disappearing suddenly. It is also capricious in that the urine may at one micturition be sanguinolent and that passed a few hours afterward may be normal. According to Mouchet this is one of the most reliable signs of the hemorrhage being of renal origin. The hematuria is usually painless, although attacks of renal colic may from time to time occur as the result of passing clots which frequently take the form of long, cylindrical casts of the ureter. Hematuria is very rarely an initial sign, and Mouchet states that in children suffering from renal neoplasms hematuria is never seen in the absence of renal tumor, as is so often the case in adults.

Inasmuch as these tumors often reach a very large size, symptoms due to compression of other organs may arise; thus the bowel may be compressed, and it is stated that in some instances the ureter of the opposite side has been obstructed. Dropsy of the lower limbs from involvement of the vena cava is frequent and ascites often develops as a result of extension to the peritoneum. Paralysis from involvement of the lumbar plexus or of the spinal cord is also not uncommon.

The progress of the disease is rapid and according to Mouchet no periods of quiescence such as are so often seen in adults suffering from malignant renal tumors ever occur in children. The average duration of the disease would seem to be from seven to eight months and the longest survival two years.

**DIAGNOSIS.** The diagnosis is almost entirely dependent on the detection of the renal tumor, inasmuch as hematuria is rare in children suffering from this disease unless a tumor is also present. The renal tumor has to be differentiated especially from tumors of the liver and tumors of the spleen and the principal difficulty arises in distinguishing between a renal tumor and a hydatid cyst from the lower surface of the right lobe. Cysts of the mesentery sometimes occur, but they are usually median in position and very mobile. Malignant disease of the kidney may be confounded with *tabes mesenterica*. Tumors of the ovary and cysts of the pancreas are rare in childhood and thus, as a rule, do not present any practical difficulties.

The efficiency of the second kidney may be determined by the chemical examination of the urine and by the injection of methylene blue. It is



only in exceptional instances that it is possible in children to use a separator to collect the urine from the two kidneys.

**TREATMENT.** The only treatment possible is the early removal of the tumor, but the results are not, as a rule, very good, owing mainly to the fact that the disease does not come under observation until well established and very often secondary deposits are already present. Recurrence is stated to occur in 81 out of 100 cases and the great bulk occurs within the first six months.

The main interest of these tumors, therefore, arises from their anatomical structure and from the light they throw on the nature of malignant disease generally.

**Arteriosclerosis of the Renal Arteries.** Josué and Alexandrescu<sup>1</sup> have investigated by modern histological methods lesions of the renal arteries in arteriosclerosis. Notwithstanding the great amount of work done on this subject since the original observations of Johnson and of Gull and Sutton there is much that is obscure in the relationship between arterial changes and chronic renal disease. Johnson, as is well known, held the view that the arterial changes were secondary to the renal lesion; whereas Gull and Sutton looked on the renal lesion as a local manifestation of widespread arterial degeneration. From that time to this different writers have held now the one view and now the other; the majority of investigators, although not agreeing with Gull and Sutton as regards the minute histology of the lesions, have on the whole supported their views that the granular kidney is merely the local manifestation of the arterial disease. This relationship applies, however, more especially to one variety of granular kidney, and it must be admitted that there are forms of primary renal disease where ultimately the kidneys may become fibroid owing to the development of fibrous tissue in the interstitial tissue of the kidney and where also arterial lesions develop secondarily. These cases are, however, different in their etiology and also in their clinical course from the ordinary granular kidney which is so frequently associated with arterial sclerosis.

The most recent writer on the subject, Jores<sup>2</sup> looks upon the changes in the renal arteries in arteriosclerosis as essentially of a degenerative character, and agrees with Gull and Sutton's theory that there is a general arterial lesion with a local development in the kidney. On the other hand, Brault considers that *interstitial nephritis* is not the consequence of a primary arterial lesion, and he holds this opinion mainly for the reason that the renal changes do not depend on the degree of arterial disease present.

Josué and Alexandrescu have investigated the subject histologically in 23 cases, and they say, like Jores, that careful distinction has to be made between the lesions of arteriosclerosis on the one hand and those of chronic

<sup>1</sup> Archiv. de méd. exp., January, 1907.

<sup>2</sup> Virchow's Arch., 1904, vol. clxxviii and 1905, vol. clxxxii.

obliterative endarteritis on the other hand. In the latter the inner coat of the vessel is thickened by an overgrowth of connective tissue traversed by a network of elastic fibers, but the well-known elastic limiting membrane is but little altered. On the other hand, in arteriosclerosis the main lesions affect the elastic and muscular elements of the vascular wall, and they think that these lesions are in part hyperplastic and in part degenerative. The hyperplasia is shown by the cleavage and splitting of the elastic lamina and the increase and thickness of the muscular coat. Foci of fatty degeneration and the disappearance of the nuclei of many of the muscular fibers are evidence of the degeneration. They think the differences observed in the lesions depend essentially on the caliber and structure of the bloodvessels involved, and these lesions are especially well marked in the case of the renal vessels and are there found to involve not only the large arteries, but also the arterioles and the capillaries of the glomeruli. They state that the large, medium-sized arteries of the kidney in arteriosclerosis always have thicker walls than normal owing to the hyperplasia of the muscular fibers and of the internal elastic lamina. The cleavage of this elastic lamina results in the presence of a number of such laminae, which may be entirely separate from one another throughout the circumference of the vessel, and between these lamellae connective tissue which in many places has undergone a hyaline degeneration is present. Further, they state that between these elastic lamellae muscular fibers with their long axes parallel to that of the vessel are to be found.

The muscular coat of the arteries is very often thickened, but in some instances it may be thinner than normal. The individual muscle cells have frequently undergone alteration, the nucleus stains badly or not at all, and the protoplasm may be full of vacuoles. The connective tissue of the outer coat is often slightly thickened. They are quite unable to find the hyaline deposit which was described by Gull and Sutton, but they have been able to demonstrate droplets of fat between the elastic lamellae and also in the muscular coat. This fatty degeneration is, however, not seen in all the vessels affected. The fine glomerular vessels may be normal, but in many instances also present signs of degeneration. The muscular fibers of the cells have lost their outline and have an indistinct nucleus, and in these vessels droplets of fat may also be found in the muscle and in the elastic laminae. In some instances they even found droplets of fat in the lumen of the vessel. The glomeruli themselves usually present the signs of hyaline degeneration and the lesions are present not only in the vascular tuft, but also in the capsule and the vascular tuft is prone to contract adhesions with the capsule. All stages up to complete fibrosis of the glomerulus can be observed. Fatty degeneration may also be detected in the capillaries of the glomeruli as well as in the arteries. The authors state that all these lesions are characteristic of true arteriosclerosis and that they are in no way of inflammatory origin, but the consequences of hyperplastic and degenerative changes.

According to these authors the distribution of the lesions in arteriosclerosis is very irregular; nevertheless the renal arteries are very frequently involved, so that in 22 out of the 23 cases of arteriosclerosis investigated changes in the large and medium-sized renal arteries were found and in 16 cases these lesions were very marked. Among the 23 cases 17 presented lesions of interstitial nephritis; in 3 cases out of these 17 the renal lesion was very marked, in 5 it was moderate, and in 9 it was slight in amount. In the remaining 6 cases the kidneys presented in 4 instances epithelial lesions with no interstitial overgrowth and in 2 instances peritubular sclerosis was present; that is to say, there was overgrowth of the interstitial connective tissue developed in a uniform degree throughout the kidney, and not presenting the irregular development that is so characteristic of the granular kidney. Although these cases presented no evidence of interstitial nephritis, yet in 5 of them considerable sclerosis of the large- and medium-sized arteries was present, and in some instances these lesions of the renal arteries were extremely marked.

The authors conclude that arteriosclerosis of the large- and medium-sized arteries of the kidney may exist without any interstitial nephritis. Thus the renal lesion cannot be looked upon as a cause of the arterial changes. Further, in the 17 cases where interstitial nephritis was present associated with the arteriosclerosis there was no correlation between the severity of the arterial lesion and the degree of development of the renal changes.

Of 9 cases where the renal changes were slight, in 8 the lesions in the renal arteries were intense. Further, in the 3 cases where the renal lesions were very marked the arterial lesions were severe in only 1 instance and, curiously enough, were least marked in the case where the renal was most marked. Thus, it may be concluded that the severity of the renal lesion is not determined by the degree of development of the arterial.

Although the renal lesions cannot be directly correlated with the arterial if the large- and medium-sized arteries are only considered, yet there is a very close relationship existing between the changes in the small renal vessels and those in the kidney elements, and the authors lay great stress on the presence of fatty degeneration in the walls of the glomerular arteries. The arterioles and the glomerular capillaries only present very slight lesions when interstitial nephritis is absent, but, on the other hand, the glomerular changes are most marked where the interstitial nephritis is most marked. Further, they think the distribution of the fibrous overgrowth in interstitial nephritis can be correlated with the changes in the capillaries and in the arterioles, whilst it cannot be associated with the distribution of the large- or medium-sized arteries.

The authors recognize two forms of sclerosis: One where the connective tissue is, so to say, superadded to the normal tissue, and the other where it replaces it. In the former the organ affected is first of all hypertrophied, but in the latter the atrophy is primary. They consider that

interstitial nephritis is a form of fibrosis where the fibrous tissue replaces the normal elements and is not superadded to them, and that the atrophy of the renal tubules and of their epithelium, together with the degeneration of the glomeruli, are the result of the vascular lesions. In early cases it is possible, they state, to see that the atrophy of the tubes and of the glomeruli precedes the fibrous overgrowth, and that they are in no sense the consequence of this fibrous overgrowth. According to this view the renal fibrosis is a direct consequence of arterial sclerosis involving the arterioles and capillaries in the glomerular system.

**Increased Arterial Tension and Renal Disease.** Increased arterial tension is closely associated with renal disease, although it is not confined to this condition. T. C. Janeway<sup>1</sup> considers that three varieties of hypertension may be recognized: One occurring in association with *arteriosclerosis*; the second, the well-known form associated with renal disease, and a third, where hypertension is present without either the existence of arteriosclerosis or of renal disease. It is, of course, most common in renal affections and especially in association with chronic interstitial nephritis. It occurs occasionally in arteriosclerosis, but not so frequently as is sometimes thought, inasmuch as investigation of the pulse with the finger is apt to mislead and increased tension may be thought to be present when there is really only thickening of the arterial wall. In the third group of cases the clinical symptoms resemble those seen in the cardiovascular type of chronic Bright's disease, but there is no evidence in these cases of any renal lesion. Janeway states that in an investigation of 131 cases where the systolic pressure was over 200 mm., 13 per cent. of the cases belonged to this third group, where neither arteriosclerosis nor renal disease was present.

In the production of high tension in arteriosclerosis it is probable that the abdominal vessels, especially those of the splanchnic area, must be involved and, further, that hypertension is not likely to be developed unless the nutrition of the heart wall is well maintained. In arteriosclerosis the coronary arteries are so frequently involved that the nutrition of the heart wall is greatly impaired, and this perhaps may be the explanation of the fact that high tension is not more often seen in association with arteriosclerosis.

The problem of high tension in nephritis is still unsolved and, as Janeway points out, this high tension cannot be explained satisfactorily by any simple mechanical or chemical theory. The lesions found in the smaller arteries are doubtless capable of producing the hypertension observed, but these lesions cannot be looked upon as the cause, inasmuch as increased tension is frequently observed quite early in the course of the nephritis, long before any anatomical changes in the heart or vessels have taken place and, hence, it is probable that the lesions found in the small

<sup>1</sup> American Journal of the Medical Sciences, January, 1907

arteries in chronic renal disease are often rather the result than the cause of the high tension. Further, as Janeway points out, an increase in the peripheral resistance due to purely mechanical causes can scarcely be looked upon as the cause of the high tension when the delicacy of the vasomotor regulating mechanism is considered. Thus, he quotes the case of a patient where the tension could not be permanently lowered by the administration of vasodilators, but notwithstanding this nitroglycerin produced well-marked temporary lowering of the blood pressure. Hence, in such a case increased vasomotor activity must have been a factor in the production of increased tension.

Many writers have thought that the high tension of renal disease was due to the primary hypertrophy of the heart, but this again cannot be looked upon as the cause of permanent high blood pressure, since with a normal vasomotor system a rise so produced would be immediately neutralized by peripheral dilatation. Janeway rather inclines to accept the theory of Loeb that the increased blood pressure may be brought about reflexly through the vasomotor system and that the peripheral stimulus is to be sought in the vascular changes in the glomeruli. The reflex splanchnic vasoconstriction would be evoked from the glomeruli and ultimately the glomerular changes would be associated with the development of the hypertrophy of the heart and the secondary changes in the arterial wall.

*The pathology of hypertension* where neither arteriosclerosis nor renal disease are present is very obscure, but Loeb has also suggested that this increased tension may also result from a vasoconstrictor reflex dependent on changes in the brain vessels, as it is known that anemia of the brain, and especially of the medulla, gives rise to a great increase in arterial tension.

In order to *treat hypertension* satisfactorily it is essential to bear in mind, as Janeway states, that "hypertension expresses an attempt of the organism to maintain an adequate speed of capillary flow through the kidney or other important organ." Hence, the presence of hypertension does not necessarily call for treatment directed to lower blood pressure. The high pressure of the circulation is characterized by several departures from the normal; thus, the diminished distensibility of the arteries causes the pulse wave to be much more sudden than normal and thus favors arterial rupture. But the danger most likely to occur is the gradual failure of the left ventricle.

Much can be done to prevent the development of hypertension by general hygienic and dietetic treatment. Rest and a milk diet may be necessary in some cases, but much can be done by mere restriction of the diet and the avoidance of all physical and mental strain. Massage and the iodides are also useful.

Janeway draws attention to the fact that formerly the discovery of the presence of high blood pressure in any given patient was looked upon as

an indication to reduce it at any cost. It is now recognized that the patient may run as great risks from excessive lowering of the tension as from its excessive height; and the treatment must be directed not merely to the height of the pressure, but by consideration of the symptoms present; in many cases a fall in the pressure marks the onset of cardiac insufficiency and is an indication for the use of *digitalis*, and Janeway draws attention to the fact that results are obtained with *digitalis* in cases of failing heart secondary to hypertension which are quite as brilliant as those seen in treatment of cases of mitral insufficiency with the same drug. He concludes that the indications for *digitalis* are the same with hypertension as without and that no blood-pressure reading should make us hesitate to administer it.

Where the symptoms of the patient depend actually on the hypertension as in some anginal seizures, nitroglycerin and other similar drugs are most efficient; venesection and chloroform narcosis may also be called for in some instances.

Edema of the lung is a dangerous complication and would seem to depend on sudden weakness of the left ventricle. Cardiac stimulants and vasodilators should be used in combination in such cases.

Janeway draws attention to the use of morphine in the cases where severe abdominal pain or intense headache are the prominent symptoms.

Janeway concludes by drawing attention to the fact that the height of the blood pressure gives no indication for treatment except along preventive lines, that hypertension is no more to be treated than a cardiac murmur, and that the treatment should be directed according to the presence of symptoms pointing to inadequate maintenance of the circulation or to the sudden occurrence of dangerous complications.

**Experimental Arterial Degeneration.** Evidence is accumulating that the lesions of arteriosclerosis are very largely dependent on toxic causes, and that the toxic agents giving rise to this degeneration also cause an increase in arterial tension by acting on the vasomotor mechanism or directly on the muscular coat of the vessels. It is now well known that adrenalin given to animals daily for a few weeks is followed by the development of calcification of the thoracic aorta, and that actual aneurysmal bulging and distinct aneurysms may in this way be rapidly produced. The lesion would seem to consist primarily in a degeneration of the muscular fibers followed by the deposition of lime salts, and the elastic tissue of the vessel wall is only involved secondarily. Extensive arterial degeneration has also been produced by the intravenous injection of nicotine, phloridzin, and the administration of lead salts and tobacco. The action of all these substances is extremely rapid, and it would seem that the results are more readily produced in old animals than in the young. Some writers have thought that the effects produced depended on the toxic action of the substances employed; others, that the degeneration was the

direct result of the increased arterial tension that most of these substances produce.

*Adrenalin*, undoubtedly, has a toxic action quite independent of its vasoconstrictor effect, and Miller's<sup>1</sup> experiments were directed to clear up the point as to whether the arterial changes produced by adrenalin were of toxic or of vasoconstrictor origin.

Thus, the injection of adrenalin is known to produce degenerative changes in the kidney and liver and, further, the subcutaneous injection is liable to be followed by necrosis of the tissues of some animals, at any rate. On the other hand, the prolonged administration of adrenalin is capable of causing a permanent rise in pressure. Miller attempted to settle this question by administering adrenalin together with nitrite of amyl, but he found that although the nitrite of amyl produced a fall of pressure under these circumstances, yet the effects of the adrenalin on the vasomotor system were still present. In other words, all that the nitrite of amyl did was to diminish but not to abolish the pressor effect produced by adrenalin, and he found that in such animals there was no gross or microscopic evidence of arterial degeneration nor any evidence of cardiac hypertrophy. It would thus seem that if a great rise of blood pressure was avoided the arterial lesions were not developed. The subcutaneous administration of adrenalin was not followed by any vascular changes, but under these circumstances also the effects in heightening the blood pressure are quite inconstant.

Intravenous injections of *nicotine* every day for six weeks produced slight but typical changes in the aorta. *Physostigmine*, which also gives a rise of pressure, administered daily in doses of 1 mg. for a period of eight weeks, also led to slight changes in the descending aorta, and it is of interest to note that *barium chloride*, which has an action very similar to that of digitalis, also led to the development of slight lesions in the large vessels, and in the case of this substance the lesions were much more confined to the intima.

It would seem from these observations that it is more probable that the arterial lesions are associated with the rise of pressure produced by the various substances used than that they are due to any toxic action.

**Renal Extracts** have been used from time to time in the treatment of *uremia* with very equivocal results. Carnot and Lélièvre<sup>2</sup> consider that renal extracts are capable of influencing both the regeneration and the development of the kidney, and that a distinct effect on the growth of the kidney can be produced by the use of such extracts. To the substances present in the kidney extract and also in the blood stream which they consider are capable of stimulating the growth of the kidney cells they give the name of nephropoietic. Their experiments were initiated as a result of theoretical considerations that when the kidney structure was

<sup>1</sup> American Journal of the Medical Sciences, April, 1907

<sup>2</sup> Archiv. de méd. exp., June, 1907

damaged by toxic agents the return to the normal could only take place if the degenerated cells were replaced by healthy ones, and that if such highly elaborated cells as those of the kidney underwent such multiplication it was probable that some chemical stimulus was at work.

The authors had previously shown that if animals were given large quantities of nitrogenous food, especially a meat diet, the renal cells underwent proliferation and, further, that the injection into the circulation of substances like urea, having a diuretic action, also had a direct action on the kidney favoring its growth and regeneration.

They obtained their so-called nephropoietic substances in the following manner: A unilateral nephrectomy was performed and then an extract of the blood or of the kidney of the animal was obtained at a time when the remaining kidney was undergoing hypertrophy. These extracts were injected into other animals and the effects on the kidney observed. Unilateral nephrectomy leads, as is well known, to a compensatory hypertrophy of the other kidney, which varies very much in amount, the degree of hypertrophy depending on the age and the state of nutrition and probably other factors. The blood of these nephrectomized animals was collected aseptically and the serum obtained after coagulation. An extract of hypertrophied kidney in salt solution was also collected aseptically. The serum and the extract were administered to healthy animals either by the mouth or by subcutaneous injection. The animals so treated presented no disturbance of their general health and their body weight did not diminish. The secretion of the urine was not materially modified and no albuminuria was produced, but according to the authors very definite results, both macroscopic and microscopic, were obtained in the kidneys, and they state that the total kidney weight as compared to the body weight underwent an increase. The injection of the blood serum was followed, they state, by proliferation involving all parts of the uriniferous tubules and also affecting the glomeruli, an intense nucleoproliferation being observed at the hilum of the glomerulus, and they regard these histological changes as evidence of the formation of new glomeruli. The uriniferous tubules also show that the epithelial elements lining them have undergone great proliferation and karyokinesis is frequently observed. On the other hand, the interstitial connective tissue shows no changes and no interstitial nephritis was ever observed.

The action of the renal extract prepared from the kidney undergoing hypertrophy is even more marked than that produced by the blood serum. They state that three weeks after the injection of such an extract distinct evidence of the formation of new glomeruli can be observed. The proliferation of the tubular epithelium is also extremely marked and in some instances the lumen of the tubes is obstructed owing to the cellular proliferation, and karyokinesis of the nuclei of the tubular epithelium is frequently to be observed. Small tubules are frequently to be seen



completely lined with epithelium and presenting appearances suggestive of the formation of new tubules.

The authors also made some observations on the action of extracts prepared from fetal kidneys, being led to these experiments owing to the rapid growth the kidneys undergo during fetal life, and the histological examination of the kidneys of animals treated by these injections of fetal kidney show a more intense proliferation even than that seen after the use either of the serum or renal extracts of adult animals.

Carnot and Lélièvre consider that these results point to the action of some specific substance owing to the limitation of the effects to the epithelial elements of the kidney. The glomerular epithelium and the tubular epithelium undergo proliferation, but no congestion, inflammation, or fibrosis of the interstitial tissue is produced. Further, they consider that there is distinct evidence that new tubules are formed as a result of budding from existing tubules, and a fusion takes place between these new tubules and the vascular bud produced at the hilum of the glomerulus, and that in this way a new glomerulus and new tubules are produced.

The authors conclude by drawing attention to the importance of these facts in the treatment of renal lesions, and this places the uses of renal extracts in the treatment of kidney disease on a different basis. If the renal extract contains a substance capable of stimulating healthy renal tissue and so leading to renal hyperplasia, it is obvious that renal extracts might be of great use in the treatment of many renal diseases, inasmuch as these are very often local and partial in their incidence on the kidney. Even in such a malady as nephritis the distribution of the lesions in the kidneys is by no means uniform.

They conclude their paper by the narration of a few cases of albuminuria where renal extract was administered. In several of these improvement was noted and the albuminuria diminished, but the results were not conclusive.

**Renal Hematuria.** Cases of profuse hematuria are seen from time to time where there is great difficulty in recognizing the cause of the hematuria, inasmuch as the usual causes, such as calculus, tuberculosis, or neoplasm, can be excluded. Some of these cases of profuse renal hematuria are dependent on the existence of renal cirrhosis, and the profuse hemorrhage occurs from the mucous membrane of the renal pelvis. Some of these cases fall into the category described by Gull under the term renal epistaxis, and the hemorrhage is perhaps dependent on the occurrence of hemorrhage into the submucous tissue of the renal pelvis. It is possible that in other cases profuse renal hemorrhage may be the result of a papillomatous or villous growth involving the mucous membrane of the renal pelvis. The presence of renal cirrhosis can usually be diagnosed; on the other hand, the presence of a papillomatous or villous growth of the renal pelvis is difficult and often impossible to recognize,

When all these causes of renal hemorrhage are excluded there still remain cases where there is reason to think the hemorrhage is derived from the kidney and yet where no physical signs can be elicited to give a clue as to its cause. In some of these cases the hemorrhage is very profuse and may be recurrent, and naturally such cases are very obscure clinically, and it has been stated that in some instances the exploration of the kidney and even the naked-eye examination of the organ after nephrectomy have failed to reveal the cause of the profuse hemorrhage.

Cases have been described from time to time where the severity of the hemorrhage has endangered the life of the patient and so has led to an exploratory operation undertaken with the suspicion of a renal neoplasm being present, and yet where nothing has been found to account for the hemorrhage.

Taddei<sup>1</sup> records a case of great interest from this point of view, inasmuch as microscopic lesions were found in a case that presented but little change to the naked eye. The patient was a woman, aged twenty-three years, who was admitted to a hospital, in Florence, in 1906, having suffered from recurrent and profuse hematuria for the last two years. The hematuria was not accompanied by any pain and lasted usually about a month. It recurred again a year later and was accompanied by intense anemia; no physical signs were found beyond slight tenderness in the region of the right kidney, and the urine presented no marked changes except the presence of red blood corpuscles in abundance. The use of the cystoscope and Luy's separator showed that the blood was derived from the right kidney. No evidence could be obtained of the presence of tubercle, as the tubercle bacillus was absent from the urine. The urinary sediment contained a considerable number of white blood corpuscles, but no actual pyuria was present. An exploratory operation was undertaken with the idea that the case might be one of renal tuberculosis, notwithstanding the absence of any bacilli in the urine. The kidney was found to be small, of a rather soft consistency, normal color, and the ureter somewhat increased in diameter. On incision, nothing was found to account for the hematuria, but the kidney substance was not quite normal. The mucous membrane of the renal pelvis, however, showed some translucent gray nodules suggesting the presence of miliary tuberculosis of the renal pelvis, and the kidney was excised under the idea that this malady was present. Subsequently to the operation there was no return of the hematuria and the patient's condition progressively improved. The injection into animals of portions of the kidney of the renal pelvis and of the ureter was not followed by the development of any tuberculosis.

On microscopic examination the renal epithelium showed signs of degeneration, especially in the convoluted tubules. The cortex of the

<sup>1</sup> *Annales des maladies des organes génitourinaires*, January, 1907.

kidney presented a number of nodular masses consisting of round cells having the structure of leukocytes. This cellular infiltration extended as far as the medullary substance and in places had led not only to the compression of the uriniferous tubules, but also to their destruction. There was some increase of connective tissue round the glomeruli resembling that seen in renal cirrhosis. The mucous membrane of the calices and of the renal pelvis contained numerous miliary nodules having the structure of lymphoid tissue, and the author attributes the hemorrhage to these lymphoid follicles that were not only present in the renal pelvis, but also in the mucous membrane of the calices and in the upper part of the ureter.

The presence of evidence of renal fibrosis suggests that these lesions of the renal pelvis may have been of an inflammatory nature, and the author is not certain whether they should be so regarded or whether the case was one of early lymphadenoma of the renal pelvis.

The point of importance in the case lies in the fact that the profuse hemorrhage was of renal origin and dependent on lesions so ill marked as only to be recognized with certainty by microscopic examination, and the author is convinced that if the kidney had only been examined by the naked eye the case might have been described under the misleading heading of essential or idiopathic hematuria. The author thinks that it is probable that all cases of hematuria where there is not a gross lesion are really dependent on the presence of some pathological process which would be revealed on microscopic examination.

Many writers, such as Senator, Israel, Naunyn, think that hematuria may be produced as the result of nephritis without the occurrence of albuminuria apart from the hematuria, and there can be little doubt that in some cases it is merely the result, as already mentioned, of renal cirrhosis. Further, it may be due, even when profuse, to the irritation caused by crystals of uric acid or of oxalic acid. All these causes, as well as microscopic lesions of the renal pelvis, must be excluded before such a cause as angioma is invoked.

The main importance of the case recorded by Taddei lies in the fact that it may be justifiable to remove the kidney for hematuria where it is not apparently grossly diseased so far as can be seen by naked-eye examination.

**Functional Activity of the Kidney.** Many methods have been elaborated in order to determine if possible the functional activity of the kidney. This is of especial importance in surgical affections where it is proposed to remove one kidney, and it becomes a matter of importance to ascertain the functional activity of the second.

Turner<sup>1</sup> has elaborated a method based on the electrical conductivity of the blood and urine and the variations which these undergo in disease.

<sup>1</sup> Edinburgh Medical Journal, April, 1907.

His observations were conducted by means of a Wheatstone bridge, an alternating current, and a telephone, and at a temperature of 65°. He concludes, from a great number of observations, that the observed resistance of normal urine amounts to about 250 ohms in his apparatus, and that the resistance depends mainly upon the salts, acids, and bases present, and of these chloride of sodium is the most important. The resistance offered by non-electrolites such as sugar, albumin, and blood may, for practical clinical purposes, be neglected, and even the effect of such a substance as urea is very small as compared to that produced by chloride of sodium. In a large number of acute and chronic diseases the resistance of the urine is greatly and constantly increased. He quotes as illustrations, croupous pneumonia, diabetes mellitus, various forms of kidney disease, pernicious anemia, etc. Turner states that even during an attack of megrim the resistance of the urine may be double the normal. He finds that the average observed resistance of normal blood is approximately 900 ohms, but that it may vary between 700 and 1600.

The resistance of the blood depends essentially on the degree of salt concentration of the blood and upon the relative number of blood corpuscles to the plasm. The greater the salt concentration the lower the resistance, but the greater the number of red cells present the higher the resistance. Hence, a blood of high resistance indicates that the proportion of salts in the blood is small or that the proportion of corpuscles is large. Evidence bearing on this can be obtained by ordinary hemocytometer observations; a high resistance of the blood, together with a low resistance of the urine, are indicative of health. In disease the resistance of the blood tends to diminish; thus in kidney disease, in chlorosis, and anemia the resistance will be found to be low, and in such a malady as pernicious anemia it may be less than half that of the normal blood.

A lowered blood resistance is indicative either of fewer corpuscles than normal or more salts or both. If the resistance of the blood and the resistance of the urine be compared, it is possible to obtain a ratio between the two—that is to say, the ratio of the electrical resistance of the blood to the electrical resistance of the urine. In health this should be approximately equal to the whole numbers 3, 4, and 5. If the index increases it indicates that the blood contains fewer salts or is richer in corpuscles, that the urine contains more salts, and that therefore the functional activity of the kidney is increasing. If the renal index diminishes, then the kidney is less efficient.

Turner quotes some cases in which this method was used and where it was distinctly of value. Thus in one case of renal tumor the hemorenal index was found to be 3 and on exploration a malignant growth involving one kidney was found and subsequently to its removal the patient made a good recovery, the quantities of the urine secreted by the opposite kidney being normal. In another instance by the use of the segregator

the urine of the two kidneys was collected separately and the hemorenal salt index of the diseased side was found to be 1.6 and on the other side 2.4, the kidney on the diseased side being affected with tuberculosis. A low hemorenal index would point to the conclusion that blood contains too great a proportion of salts and the kidney too small a proportion, and hence that the renal action is inefficient. Turner considers that any index below 3 should be regarded as abnormal and suspected and that an index below 2 is to be looked upon as serious. Further observations will be required in order to determine whether this method is really available and accurate enough for clinical purposes.

**Hydremia.** Bence and Sarvonat<sup>1</sup> made some observations experimentally on the relation of hydremia to renal disease. In renal disease two forms of hydremia may exist: one a hydremic plethora dependent on the retention of water and the second where the watery state of the blood is merely dependent on the loss and diminution of its proteid constituents. Diminution in the amount of proteid in the blood is probably only in part dependent on the loss produced by the albuminuria. It is probably also largely due to the excessive destruction of proteid matter owing to the deranged metabolism present in renal disease. Further, it has been shown that after double nephrectomy the blood may be hydremic and poor in proteid matter, although under these circumstances there is no loss through albuminuria and the hydremia must be looked upon as due to the absorption of water from the tissues.

These authors have compared the quantity of water in the blood in normal animals and after double nephrectomy, and they show that in normal animals allowed to eat and drink freely the fluid content of the blood remains constant. During starvation the variations are very steady, the quantity diminishing slowly and then remaining constant. The ingestion of measured quantities of water only leads to temporary changes in the fluid content of the blood. After double nephrectomy, on the other hand, different results are obtained; thus, if such an animal is allowed to eat and drink freely there are great fluctuations in the fluid content and the same is seen in a starved animal that is allowed to drink. The giving of definite quantities of water to a nephrectomized animal is followed by sudden changes in the fluid content of the blood, the increase so produced gradually disappearing as the weight of the body diminishes.

In the nephrectomized animal the body weight undergoes a steady diminution dependent largely on the loss of water by other channels, and yet in these animals the blood becomes more watery. This is a temporary phenomenon, and with the progressive loss of weight the blood becomes again more concentrated. If such an animal is allowed to take a considerable quantity of water a condition of hydremia is produced

<sup>1</sup> Revue de médecine, July, 1907

and the giving of a quantity of water sufficient to cause the body weight to return to its normal amount leads to a very considerable hydremia. They consider that hydremia cannot be the cause of the dropsy of renal disease, owing to the fact that hydremia may occur at the expense of the water content in the tissues when no fluid is given by the mouth, and that the hydremia of renal disease is really dependent on the alteration of the composition of the blood produced mainly by the retention of salts, and that, therefore, if the water cannot be obtained from the alimentary canal it will be withdrawn from the tissues, and that this is the explanation of the experimental results obtained in nephrectomized animals. It would seem, therefore, that the hydremia of renal disease cannot be looked upon merely as a result of deficient elimination of water by the kidney, but that it is of more complex origin and dependent on the salt content of the blood being abnormally high.

# SURGERY OF THE EXTREMITIES, FRACTURES, DISLOCATIONS, TUMORS, SURGERY OF JOINTS, SHOCK, ANESTHESIA, AND INFECTIONS.

By JOSEPH C. BLOODGOOD, M.D.

## SHOCK AND HEMORRHAGE.

SURGICAL physiology is rapidly taking a place of importance equal to surgical pathology. Clinical and experimental investigations on shock, the surgery of the respiratory organs, and abdominal pain are examples of its recent advances.

In the two most recent American text-books of surgery<sup>1</sup> special chapters for the first time appear on surgical physiology. The majority of subjects discussed and the literature presented in these two chapters have been mentioned in the previous numbers of PROGRESSIVE MEDICINE.

The most important contribution of the year on the subjects of shock and hemorrhage is the direct transfusion of blood from one human being to another by arteriovenous anastomosis.

*Vessel suture* has been established by the experimental work of Alexis Carrel<sup>2</sup>, who is now carrying on his work in the Rockefeller Institute in New York. Adopting Carrel's method, Crile, of Cleveland,<sup>3</sup> established, first upon animals and then upon human beings, that the *direct transfusion of blood* can be accomplished quickly and without danger of thrombosis and embolism. Later Crile devised a tube which facilitates arteriovenous anastomosis. This he demonstrated before the Clinical Society of Surgery last October, and described it in the September number of the *Annals of Surgery*. In Baltimore, Watts, late Resident Surgeon of the Johns Hopkins Hospital, now Professor of Surgery in the University of Virginia, has performed in numerous cases direct transfusion.

There is no doubt that it is the most efficacious treatment for all forms of hemorrhage. In acute hemorrhage it saves life by immediately restoring the lost blood, both in quantity and quality, and, as this blood is of value for a few days, the organism has time to reproduce the lost corpuscles. At the present day every surgeon should be familiar with this technique.

<sup>1</sup> Keen's Surgery (Surgical Physiology, Crile), vol. i, p. 79, and Bryant and Buck's American Practice of Surgery (Surgical Shock, Bloodgood), vol. i, p. 463.

<sup>2</sup> Johns Hopkins Hospital Bulletin, 1907, vol. xviii, p. 18.

<sup>3</sup> Annals of Surgery, September, 1907, vol. xli, p. 329.

In chronic hemorrhages, for example, those observed from the large intestine, it not only temporarily changes the secondary anemia, but the foreign isotonic blood must give something which increases the coagulability of the blood of the receiver, because the hemorrhages cease.

Direct transfusion should be tried in typhoid hemorrhage and in obstructive jaundice with slow coagulation time. It has proved to be of no value in pernicious anemia, leukemia, and other blood diseases. A priori, it is only a temporary substitute, and if the blood-producing tissues are diseased it has no apparent effect. So far it has not proved of value in infections.

The future possibilities of direct transfusion may be immense. Immunity established in one individual may be transmitted to another. It is possible that through this channel malignant disease may be treated.

Direct transfusion of blood should not be used indiscriminately. That there may be thrombosis with embolism due to mixture of the blood is suggested by the recent work of Ludvig Hektoen.<sup>1</sup> The following is a direct quotation from Hektoen:

"By means of a delicate and highly refined technique, Crile recently has practised direct transfusion of blood from normal to diseased human beings, and with marked apparent success, so that it is not unlikely that the practice of transfusion may increase. The common occurrence of isoagglutinins in human serum suggests that under certain special conditions homologous transfusion might prove dangerous by leading to erythrocytic agglutination within the vessels of the subject transfused. It has not been feasible to conduct animal experiments upon this point because of failure to demonstrate isoagglutinins in the serum of suitable animals. It may be pointed out, however, that the possible danger here indicated can be avoided by the selection of a donor whose corpuscles are not agglutinated by the serum of the recipient, and whose serum does not agglutinate the corpuscles of the latter; that is to say, donor and recipient should belong to the same group, and preferably to Group I or II. The actual relation *in vitro* of the sera of prospective donors and the recipient to the respective corpuscles are readily determinable in a short time in the manner outlined in the foregoing."

I have mentioned before the intravenous injection of adrenalin-salt solution for shock and sudden death during anesthesia from acute dilatation of the heart. Crile and Dolley<sup>2</sup> present a second contribution on an experimental research into the resuscitation of dogs killed by anesthetics and asphyxia, and conclude that even after apparent death in which the heart beat has ceased resuscitation is possible with the employment of adrenalin.

<sup>1</sup> The Journal of Infectious Diseases, June, 1907, iv, No. 3, pp. 297-303.

<sup>2</sup> Journal of Experimental Medicine, December, 1906, vol. viii, p. 714.



In the technique Ringer's solution is employed: an artery is selected, and after the solution has started adrenalin is introduced into the rubber tube with a hypodermic syringe so that it reaches the heart in concentrated form. Before the Clinical Society of Surgery, in Cleveland, I had the opportunity of witnessing successful experiments of this kind.

Crile's conclusions are as follows:

1. Animals after death from chloroform, ether, or asphyxia up to five minutes were uniformly and readily resuscitated, provided that the full technique which has been described was applied; up to ten minutes there was an occasional failure; beyond ten minutes consciousness was rarely restored, and the proportion of successes in the resuscitation of the circulation and the respiration diminished with the lapse of time; after twenty-three minutes in adult dogs and thirty-five minutes in puppies complete return of circulation was not accomplished.

2. After death from chloroform and ether animals were more readily resuscitated than after death from asphyxia.

3. Resuscitation, if successful, occurred within one minute after the administration of adrenalin in the majority of instances; it rarely occurred after an interval greater than three minutes.

4. The greatest difficulty to be overcome was clotting. The probability of clotting increased in direct ratio with the lapse of time after death. Cardiac trauma predisposed to clotting.

5. The younger the animal, up to certain limits, the more readily it was resuscitated.

6. Any artery may be used for the infusion, though the advantage is probably slightly in favor of the carotid. The infusion should be directly toward the heart.

7. The probable success of resuscitation is greater in inverse relation to the lapse of time after death: a rapid rise in the arterial pressure is attained by arterial infusion with a therapeutic dose of adrenalin, together with good artificial respiration and the avoidance of unnecessary cardiac trauma by massage. All artificial aids should cease as soon as the functions are competent.

Sudden collapse during anesthesia fortunately does not take place very often. It may also occur later, after the operation and anesthesia. Surgeons should be prepared for it.

The factors in resuscitation are artificial respiration, cardiac massage, and intra-arterial salt infusion with adrenalin. The most important factor is the adrenalin and the increased blood pressure in the coronary arteries affected by the salt solution. Cardiac massage has its dangers and should be very carefully employed. Compression of the chest in the plane of the diaphragm over the heart, a few times and slowly, shortly after the adrenalin has been introduced, is sufficient. Direct cardiac massage is dangerous.

Cardiac massage in apparent sudden death has been employed. In

recent literature there are papers by Green<sup>1</sup> and Conkling.<sup>2</sup> Successful cases are recorded even after direct massage of the heart. In view of Crile's experimental work this should be employed with greater care.

Butler<sup>3</sup> gives his favorable practical experiences with adrenalin in salt solution as a cardiac and vasomotor stimulant. Potts<sup>4</sup> and Bennet<sup>5</sup> call attention to the dangers of adrenalin, even when used externally on the mucous membrane of the nose or genito-urinary tract. There is no doubt that adrenalin is a dangerous drug and should always be used with caution.

Toubert<sup>6</sup> discusses *calcium chloride* as employed in hemorrhage to increase the coagulability of the blood. In my experience calcium chloride should not be given subcutaneously. Such injections are usually followed by abscess. The best substitute is *calcium lactate*, but this is not free from danger, and should only be given in emergencies. Thayer<sup>7</sup> reports a case in which an abscess formed in the breast and axilla after a subcutaneous infusion of a 1 per cent. solution of calcium lactate in salt solution. It is interesting to note that when the abscess was incised and drained diffuse calcification of the breast and axillary glands took place, apparently due to the effect of the iodine on the calcium in the tissue, because when it had disappeared the calcification could be reproduced by reintroducing iodoformized gauze.

In a recent observation of my own, a case of typhoid perforation complicated with hemorrhage, we gave, during operation, a subcutaneous infusion of 500 c.c. of a 1 per cent. solution of calcium chloride (the lactate was not available). An abscess due to necrosis slowly developed and the entire pectoral fascia sloughed. The wound has been very slow in healing. Sladen and Hinman<sup>8</sup> in the medical wards of the Johns Hopkins Hospital have demonstrated, in cases of jaundice and typhoid fever with diminished coagulation time, that better results are obtained by administering calcium lactate by mouth or rectum in doses of 10 grains every four hours than by larger doses. This treatment should always be given preliminary to operation in cases of jaundice. In my hands it has been very satisfactory.

A very interesting historical review on infusion and transfusion is presented by Köhler.<sup>9</sup>

**Hemophilia.** One never knows when this rare disease will present itself. This summer, a boy was admitted to the surgical clinic of the Johns

<sup>1</sup> Lancet, December 22, 1906.

<sup>2</sup> New York and Philadelphia Medical Journal, September 2, 1905.

<sup>3</sup> Lancet, March 3, 1906.

<sup>4</sup> Journal American Medical Association, October 13, 1906.

<sup>5</sup> Ibid., November 17, 1906.

<sup>6</sup> Zentralbl. f. Chir., 1906, vol. xxxiii, p. 427.

<sup>7</sup> Johns Hopkins Hospital Bulletin, February, 1906.

<sup>8</sup> Ibid., June-July, 1907, xviii, p. 207.

<sup>9</sup> Zentralbl. f. Chir., 1906, vol. xxxiii, p. 613.

Hopkins Hospital almost exsanguinated from continuous oozing from a wound of the foot. We could obtain no history of hemophilia in his immediate ancestors. He was an only child, and his mother had always observed that, on the slightest bruise, he would get a black-and-blue spot. The hemorrhage could be checked for a few hours at a time by pressure and the ordinary styptics. Dr. Miller tried human blood in the wound without effect. Calcium lactate was given by mouth and per rectum. He was kept absolutely quiet with small doses of morphine by mouth. We were afraid to give him a hypodermic or prick his ear for a blood count, and I felt that the dangers of a wound necessary for direct transfusion of blood were greater than the good that could be accomplished. It is encouraging and also of great interest that the cases reported in the literature generally get well, even though they have reached an almost moribund state from the loss of blood. There seems to be a tendency to spontaneous recovery, and Weil<sup>1</sup> states that the prognosis is better in the acquired than in the congenital form of the disease. This boy recovered. In addition to the ordinary measures we employed milk per rectum, suggested by Solt,<sup>2</sup> who claims that milk contains so many salts that it is better than any single one and gives the blood what it requires to increase its coagulability. Milk is of no value if given by mouth, because it is changed by the gastric juices. Whether it was of any value in this case it is hard to say, as so many local and general measures were employed.

**Surgery of the Bloodvessels.** For the first time as far as I know an entire journal in the English language has been devoted to surgery of the vascular system.<sup>3</sup>

The contribution by Watts<sup>4</sup> has been published before. This is a very complete and interesting historical review, and is followed by the author's experiments on dogs, in which he used Carrel's method of suture. There are a number of illustrations of successfully sutured vessels.

There is another interesting historical review and summary of the results of circular suture and the transplantation of vessels by Stich, Makkas, and Dowman.<sup>5</sup>

A successful suture of bloodvessels must approximate intima to intima, be secure against secondary hemorrhage, and not be followed by thrombosis or stricture. The question of lateral suture was solved by Jassinowski in 1889, the circular suture by invagination by Murphy in 1897, and by Payr with the employment of a soluble magnesium prothesis. To Carrel belongs the credit of a successful circular suture without invagination and without a prothesis. Carrel changes the circular form of the end of the divided vessels into an equilateral triangle by passing

<sup>1</sup> *Zentralbl. f. Chir.*, 1907, vol. xxxiv, p. 509.

<sup>2</sup> *Ibid.*, p. 39.

<sup>3</sup> *Annals of Surgery*, September, 1907, vol. xlv.

<sup>4</sup> *Johns Hopkins Hospital Bulletin*, May, 1907.

<sup>5</sup> *Beiträge z. klin. Chir.*, 1907, vol. liii, p. 113.

and tying three sutures through both vessels at equal distances. When two of these sutures are stretched the ends of the vessels come together in a straight line and are approximated with a continuous suture. Very fine needles and fine silk are employed and the thread and tissues are moistened with vaselin.

I have had the opportunity on three occasions to witness Carrel's work in the Rockefeller Institute in New York.

It is time now that the accomplished results of experimental vessel suture and transplantation should be applied to practical surgery. Lexer made this statement before the last German Surgical Congress<sup>1</sup> and demonstrated his patient. Here there had been a traumatic arteriovenous aneurysm from a stab wound in the popliteal space. The operation was performed eight weeks after the injury: excision of the artery and vein was done with immediate end-to-end suture of both. He used Payr's soluble magnesium prothesis. In a second case a true aneurysm of the axillary artery was excised. The defect was too great for suture. For this reason 8 cm. of a branchless portion of the long saphenous vein was substituted. The patient died five days later. The autopsy showed a successful suture, but a thrombosis of the axillary artery above due to too firm clamping on a diseased arterial wall.

The number of successful cases is small. They are collected by Watts and Stich, Makkas, and Dowman.<sup>2</sup>

In the *Annals of Surgery* already referred to there are a number of contributions on vessel suture for injury and for aneurysm. To Matas, of New Orleans, belongs great credit for the application of suture in the treatment of aneurysm.

For thrombosis and embolism of large peripheral vessels arteriotomy should be performed, the clot removed, and the vessel sutured. This is discussed by Stewart, of Philadelphia. Lilienthal<sup>3</sup> describes an end-to-end arteriovenous angiorrhaphy, the first in which the artery has been anastomosed with the vein without a corresponding counter-anastomosis of vein into artery. The operation was not successful. In this article one will find references to many of Carrel's publications.

## INFECTIONS.

A treatment which is becoming universal for all acute and chronic infections accessible to its application is that now known as *Bier's induced hyperemia*. In *PROGRESSIVE MEDICINE*, December, 1906, p. 239, I discussed this treatment for the first time extensively with illustrations of the elastic bandage, the various cups and jars, and the vacuum apparatus. During the last year the favorable reports in the literature of all

<sup>1</sup> *Zentralbl. f. Chir.*, 1907, vol. xxxiv, Supplement, No. 31, p. 12.

<sup>2</sup> *Loc. cit.*

<sup>3</sup> *Annals of Surgery*, January, 1907, vol. xlv, p. 1

languages have multiplied. My personal experience with the method has been such that I can recommend it. It is not complicated; the patients can be instructed to use it themselves.

A few examples of my own will illustrate methods and results. A physician received a contused and lacerated wound over the anterior surface of the leg, which healed slowly. Three weeks later, the wound still being open, he attended a case of erysipelas; shortly afterward he noticed redness of the skin, great edema and swelling of the calf, pain, and fever. I saw him on the evening of the third day; the temperature was 103.5°; the entire limb below the knee was swollen and edematous; there was but a small wound in the skin filled with granulation tissue; the area of erythema extended almost to the knee and ankle and half-way around the leg; the leg was painful and very tender; the leukocytes were 15,000; there was no ascending lymphangitis; the glands in the groin were tender. The clinical picture was that of a streptococcus dermatitis with beginning cellulitis. He was placed in bed with the leg elevated and covered with a wet solution and an ice-cap; a Bier elastic bandage was placed around the thigh. Within two hours pain was relieved; the temperature was 99° next morning; the condition began to subside at once and rapidly, then gradually; at the end of two weeks a small incision evacuated a collection of pus beneath the skin below the wound.

Compared with similar cases without the use of the elastic band, the pain was more quickly relieved, the inflammation checked more promptly, and the resultant purulent collection less. This patient wore the bandage for two weeks, day and night, removing it every six or eight hours, with an interval of two hours off. In the first treatment the bandage was worn continuously for ten hours.

Dr. Gamble, of Baltimore, gives me the following case: An adult consulted him for an infected toe with erysipelas extending up the leg, beyond which there was beginning lymphangitis; locally there were pain and edema, generally fever. The bandage was placed around the thigh about twelve hours after the onset, with immediate relief of discomfort, checking of the extension of dermatitis, and rapid subsiding of the inflammation. In this case the bandage was placed at first so tightly that it produced edema of the limb up to the bandage; this disappeared when the bandage was changed ten hours after it was first put on. Both physician and patient had had previous experience with a similar infection, and were impressed with the more rapid improvement after the use of the elastic bandage.

In the following cases I am convinced that the venous stasis and local hyperemia produced by the bandage acted favorably: Infections of the fingers and finger nails, slight infections after suture of superficial wounds and tendon sutures, compound fractures, infections of the stump after amputation for crushing injuries, infected chronic leg ulcers. It is, therefore, very useful in minor surgery in dispensary practice. I have

employed it in all forms of acute and chronic arthritis. The cups have been used in all fistula and sinus formations, in furuncles, but up to the present time I have not had an opportunity to use it for carbuncle, nor in acute lactation mastitis. In all these and other infections the larger experience of the literature records favorable results.

It is of the utmost importance to remember, as pointed out by Bier, Lexer, and others, that the elastic bandage or the vacuum jar is not a cure-all, but only a part of the physician's treatment of infections. In lighter cases its employment alone may be sufficient; in graver infections the ordinary treatment of incision should be used. In conjunction with Bier's hyperemia experience has demonstrated that the incision to relieve tension or evacuate pus may be smaller, and packing of such wounds has been universally discarded.

Fig. 1 shows a bilateral post-typhoid osteomyelitis of the lower rib. When I first saw the patient there was diffuse induration, pain, and great tenderness. Under the application of the vacuum jar (Fig. 2) an abscess quickly developed, with relief of pain and tenderness; small incisions were made and then the small cup followed by the large jar was employed. The patient now has two small sinuses, which are still discharging. Whether a permanent cure will be accomplished I cannot say at this time. If this result does take place I will consider it a triumph of hyperemia. So far in my experience I have never observed a spontaneous cure of post-typhoid osteomyelitis, and, to cure the disease, it has always been necessary to resect two or more ribs.

Riedl,<sup>1</sup> in recording his experience with obstructive hyperemia, states that he uses an ordinary calico bandage instead of the rubber one. Joseph<sup>2</sup> from Bier's clinic gives a very interesting discussion on the nature of inflammation in relation to hyperemia, which differs very little from that in the fifth edition of Bier's book just published. He emphasizes the fact that inflammation is a natural reactive process of the tissues to combat infection and produce local immunity, just as there are changes in the blood to produce general immunity. The experiments on the healing of cartilage by Donati and Delfino<sup>3</sup> show the effect of hyperemia on this process. Incisions were made in the ear of rabbits through skin and cartilage; the wounds were closed; hyperemia was established on one ear by collodion. At later examinations the healing of the cartilage on the obstructed side was more rapid, and the regeneration of the cartilage greater.

Ritter,<sup>4</sup> in his paper on the practical importance of the natural relief of pain, is of the opinion that pain and inflammation cannot be explained by tension alone, but are due to the irritation by the products of the

<sup>1</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 828.

<sup>2</sup> Deutsch. Zeitschr. f. Chir., 1907, lxxxvii, p. 425

<sup>3</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 945.

<sup>4</sup> Ibid., p. 150.

infectious agent, and that in passive hyperemia these products are neutralized. In this way he explains why hyperemia which increases tension relieves pain.

No contribution can compare with Bier's book as to the details of his treatment, and as yet nothing of consequence has appeared in English.



FIG. 1



FIG. 2

I am of the opinion that this book should be translated and made accessible to the general practitioner.

Adami's revised and enlarged reprint of his article in Allbutt's *System of Medicine*, on "Inflammation and Introduction to the Study of Pathology," has just appeared (The Macmillan Co., New York). In the prospectus the author believes that a knowledge of the inflammatory

process is the foundation of all pathology, and he has here brought together all the data known to him bearing upon the subject, including some very recent ones, such as Wright's researches upon opsonin and Bier's treatment of inflammation by induced hyperemia. This is a book which should be read by every practitioner.

### ANESTHESIA.

**Scopolamine-morphine Narcosis.** Schneiderlin, in 1900, introduced this method. In *PROGRESSIVE MEDICINE*, December, 1903, I discussed the literature very fully and at that time came to the conclusion that the employment of large and repeated doses of scopolamine and morphine was sufficiently dangerous to contra-indicate its use. At that time the experience with smaller doses as a preliminary to ether or chloroform narcosis was not sufficiently great to estimate its value.

Grimm<sup>1</sup> now reports on the experience in Kümme's clinic in Hamburg-Eppendorf based upon 2850 cases during a period of two and one-half years. Practically since December, 1903, every patient, except those younger than sixteen years, have received, preliminary to the general narcosis, a hypodermic injection of scopolamine and morphine. They have employed scopolamine in the dosage of 0.0005 gram ( $\frac{1}{2000}$  grain) and morphine 0.01 gram ( $\frac{1}{100}$  grain). Each drug is given separately one to one and one-half hours before operation. It is of the utmost importance that the solution of scopolamine be freshly made every two days. It can be prepared by taking *scopolamine* (Merck) 0.005 gm. to 10 c.c. of water. Such a solution, therefore, contains ten doses of 1 c.c. each. This solution should be kept in a dark, dry, cool place.

Grimm calls attention to the fact that, although the first hundred cases of narcosis with repeated large doses of scopolamine and morphine alone were successful, further experience demonstrated complications and fatalities sufficient to contra-indicate its use in such doses.

The experience of Kümme's clinic with a dose of each drug not in itself dangerous, it seems to me, clearly proves that it is a valuable adjunct to general anesthesia, and after reading this article I feel that I can recommend it. The patients are relieved of the mental anxiety during transportation to the operating-room. With the exception of alcoholics, there is no excitement; in full narcosis no increased secretion and no asphyxia. After the operation the first pain and discomforts are deadened: nausea and vomiting are rare, and Grimm states that post-operative pneumonia is less frequent.

This report impresses me that scopolamine-morphine in hypodermic injections will prove to be a better adjunct to general narcosis than a

<sup>1</sup> Beiträge zur klin. Chir., 1907, lv. p. 1.



combination of atropine and morphine. Gauss<sup>1</sup> employs it during labor. Busse<sup>2</sup> reports on the combination of this method with lumbar anesthesia in gynecological operations. Newell,<sup>3</sup> of Boston, reports favorably on scopolamine-morphine in obstetrics. He uses  $\frac{1}{16}$  grain of scopolamine hydrobromide (Merck) and morphine  $\frac{1}{4}$  grain; in some cases the dose was repeated in one to two hours.

The literature on this method of anesthesia has collected since my last report in 1905, and I find twelve references, in addition to those already quoted, in my card-index, prepared and kept for me by Mr. Schapiro.

**Spinal Anesthesia.** It is rather interesting to note that the number of references to spinal anesthesia in the last three years far exceeds those to local or general anesthesia. This is due to the fact that since Bier's<sup>4</sup> publication on his improved method new interest has been awakened. In this country, due, I am sure, to the great improvement in the administration of ether, interest in local and spinal anesthesia has decreased.

In the German Surgical Congress<sup>5</sup> in April, 1905, Bier and his assistant Dönitz describe the improvement in their technique in spinal anesthesia and recommend stovaine and adrenalin injected together. Bier reported 300 cases with 4 per cent. failures. At the same time Fuster, from von Hacker's clinic, recommends tropacocaine without adrenalin. One year later Bier<sup>6</sup> in reporting 1000 cases changes in favor of tropacocaine without adrenalin. The dose is 0.05 gram tropacocaine. Before the drug is introduced spinal fluid must flow easily from the hollow needle. To enlarge the field of anesthesia Bier recommends an increase of the fluid in which the drug is dissolved up to 6 to 8 c.c. The best fluid for dilution is that which flows from the needle. The effect is also increased by raising the pelvis (Trendelenburg position).

Oehler<sup>7</sup> reports on an experience with 800 cases which in a foot-note had increased to 1000 before the publication of his article. After an experience with many drugs, especially stovaine, they now, similar to Bier, recommend tropacocaine. This latter, however, has the disadvantage of a shorter and, in some instances, less complete anesthesia. In their experience it has not been satisfactory in laparotomies. To increase the anesthesia above the plane of the pelvis one must elevate the pelvis. This, even with tropacocaine, has its complications and dangers. In using tropacocaine it should be prepared in a fresh solution. The commercial preparation which is mixed with adrenalin may decompose. In some cases adrenalin also in fresh solution is added.

<sup>1</sup> Archiv f. Gyn., 1906, lxxviii, Heft 3.

<sup>2</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 25.

<sup>3</sup> Surgery, Gynecology, and Obstetrics, August, 1907, v, p. 153

<sup>4</sup> Ibid.

<sup>5</sup> PROGRESSIVE MEDICINE, December, 1905, p. 173.

<sup>6</sup> Mediz. Klinik, 1906, p. 1120.

<sup>7</sup> Beiträge z. klin. Chir., 1907, lv, p. 273.

Kurzweily,<sup>1</sup> from Hofmeister's clinic in Stuttgart, writes that after a large and long experience in which all the different drugs have been used, including tropacocaine, they have given up the method. It has failed them also in some of those cases in which they preferred not to give a general anesthetic. During the same time a comparison of over 300 spinal anesthetics with over 600 general anesthetics has convinced them that the dangers and discomforts of the latter are distinctly less. They have observed pneumonia to also follow spinal anesthesia.

Other literature need not be given, as I am impressed that, with the great improvement in general anesthesia, at least now, spinal anesthesia is not a competitor. Personally, I have never employed it.

**Local Anesthesia.** The recent literature is concerned chiefly with the employment of new drugs, substitutes for cocaine, especially stovaine, and with combinations with adrenalin.

Schleich,<sup>2</sup> in the new, fifth, edition of his book still prefers cocaine, but adds alypin; the latter increases the local effect of cocaine as an anesthetic and diminishes its general toxic effect. He recommends the following three solutions:

	I.	II.	III.
Cocaine . . . . .	0.1	0.05	0.01
Alypin . . . . .	0.1	0.05	0.01
Sodium chloride . . . . .	0.2	0.02	0.02
Distilled water . . . . .	100.0	100.00	100.00

In my own experience I still use very weak solutions of cocaine, about equivalent to Schleich's third solution. I have given up adrenalin on account of the danger of secondary hemorrhage, which is also mentioned by Sazzyn.<sup>3</sup>

When large quantities, even of the weakest solutions of the cocaine solution, must be used, there is always some toxic effect, so far, in my experience, not dangerous, but enough to make it imperative to keep the patient quiet for twenty-four hours. In aged people there may be delirium, and if they are not watched they will get out of bed and walk about. Local anesthesia in laparotomies for grave lesions like intestinal obstruction, advanced carcinoma of viscera, etc., does not prevent postoperative pneumonia, although this is less frequent than after a general anesthetic. This is explained by the fact that such pneumonias are embolic from thrombosed vessels in the region of the disease.

Further experience has also demonstrated that the opening of the abdomen, even under cocaine anesthesia, is by no means devoid of shock. This has been proved by experiments on animals. In a rabbit the visible peristalsis of the cecum disappears the moment the peritoneum is opened. For this reason there is an element of danger in performing laparotomy,

<sup>1</sup> Beiträge z. klin. Chir., 1907, liv, p. 735.

<sup>2</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 9.

<sup>3</sup> Ibid., p. 626.

for example, herniotomy, on patients suffering from grave cardiac lesions, even under local anesthesia. In the hands of one of my colleagues sudden death took place as the sac of the hernia was opened. This patient was suffering with chronic endo- and myocarditis. Apparently good compensation had been established after a rest in bed for three weeks. The patient experienced no pain, but when the peritoneum was opened the pulse became very rapid, intermittent, and finally stopped. He did not react to an intravenous injection of adrenalin-salt solution. We know from Lennander the sensibility of the parietal peritoneum. In this death there were probably two factors—the general toxic action of the cocaine and the reflex afferent-nerve impulse from the sensitive peritoneum.

The field of local anesthesia is, undoubtedly, increasing. One who has mastered the details of technique and employs very weak solutions of cocaine, and who knows the positions of the peripheral sensory nerves and the sensibility of the different tissues and organs, will be able to perform in a most satisfactory manner many operations. There is no question that if the operation can be done without pain under local anesthesia it is much safer than under general narcosis.

The most interesting contributions to the knowledge of the sensibilities of tissues have been contributed by Lennander.<sup>1</sup> The earlier works of this surgeon I<sup>2</sup> have discussed.

**Chloroform Anesthesia.** This drug is constantly losing ground, except in obstetrical practice, as a method of general anesthesia. In recent literature the chief references are to early and late deaths after chloroform, the effect of chloroform on the viscera, the importance of giving this drug in exact doses, its mixture with oxygen and ether to diminish its dangers. All of these subjects have been previously discussed in *PROGRESSIVE MEDICINE*. I find nothing new to add.

In my own experience I find that there are occasions when chloroform is indicated, either as the only anesthetic or, now and then, in combination with ether. In the Rochester Clinic, in 1905, Alice Magaw<sup>3</sup> found it necessary to give chloroform 133 times as compared with ether 2847—a proportion of about 1 to 20. This is a larger proportion than that in which I found it necessary to use chloroform.

Alcoholics with thick necks take ether at first badly; and the addition, now and then, of a few drops of chloroform during the beginning of the anesthetic lessens the stage of excitement and the muscular rigidity which produces cyanosis. In cases of peritonitis and intestinal obstruction chloroform, at least until the stomach is thoroughly washed out, is the better anesthetic.

<sup>1</sup> Mittheilungen a. d. Grenzgeb. d. Med. u. Chir., 1906, xv, p. 465.

<sup>2</sup> International Clinics, 1907, i, Seventeenth series, p. 277, and in American Practice of Surgery, Bryant and Buck, i, p. 463.

<sup>3</sup> Surgery, Gynecology, and Obstetrics, December, 1906, iii, p. 795.

**Ether Anesthesia.** It is gratifying to observe the general employment of the drop method on the open cone, first advocated in Germany, and which I have recommended in *PROGRESSIVE MEDICINE* since 1900.

In this country the credit for perfection of the method and its popularization belongs to Alice Magaw,<sup>1</sup> in Mayo's clinic. One should read her brief, but clear review of 14,000 surgical anesthetics.<sup>2</sup> It is very interesting that the method in which the expert gets the best results is not only the simplest of all, requires the least paraphernalia, but is the method which in the hands of the inexperienced is the least dangerous. Ether given continuously in drops on a small open cone is now the method of choice, and when given by an expert limits the field of local anesthesia, and, in my opinion, prohibits the use of spinal anesthesia. I would make but one addition—the preliminary hypodermic injection of small doses of scopolamine and morphine. With this, in 73 cases, Alice Magaw could demonstrate no improvement over morphine alone in a dose of  $\frac{1}{4}$  grain thirty minutes before operation. Since, however, the recent communication of Grimm<sup>3</sup> I would suggest its trial in this country.

**Ethyl-chloride Narcosis.** As a preliminary to ether narcosis many expert anesthetists are using ethyl-chloride sprayed into a closed mask. It is the method of choice in the Pennsylvania Hospital in Philadelphia, and is employed by Davis, an expert anesthetist in Baltimore. Its only advantage is that it shortens the time necessary to produce full narcosis, which is comparatively slower in the drop method. The fatalities, however, reported in the literature<sup>4</sup> are sufficient to contra-indicate its general employment, except by the expert, and personally by him only in a few and well-selected cases.

## FRACTURES.

In the two most recent American contributions to this subject by Eisendrath<sup>5</sup> and Duncan Eve,<sup>6</sup> the pages devoted to the general recognition and treatment of fracture and to repair, callus formation, are too few. In the recognition and treatment of fractures in general, modern experience and investigation have changed many of the older views. The *x*-rays have revolutionized diagnosis. The older opinion as to absolute immobilization is gradually being replaced by the more rational and so-called functional treatment, and the indications for operative intervention are now more clearly defined.

The treatment of fractures in this country, both in private practice and

<sup>1</sup> Loc. cit.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, December, 1906.

<sup>3</sup> Loc. cit.

<sup>4</sup> Luke, *Lancet*, May 5, 1906; Hoton, *Zentralbl. f. Chir.*, 1906, xxxiv, p. 717; Knight, McCardie, *British Medical Journal*, March 17, 1906.

<sup>5</sup> Keen's Surgery, ii, p. 75.

<sup>6</sup> American Practice of Surgery, Bryant and Buck, iii, p. 63.

in hospitals, either in the out-patient departments or in the wards, can be criticised. The average surgeon, young or old, takes little interest in the non-operative methods. His enthusiasm is lost after the first inspection of the *x*-rays, the reduction, and first dressing of the fracture.

I have called attention to these facts before, but recent experience and the contributions to the literature justify more or less repetition.

**Functional Treatment of Fracture.** This term can be applied to the after-treatment of all fractures, whether subjected to operation or not. It emphasizes the importance of all means to preserve good circulation and muscle tone in the injured limb, and to aid proper callus formation. In the functional treatment immobilization and fixation are only employed to a sufficient degree to keep the fragments in place. The tendency to dislocation after reduction in many fractures, for example, Colles', is usually exaggerated in the mind of the surgeon. In the last two years I have given up any fixation dressing in Colles' fracture after the second week. The *x*-ray studies have demonstrated no tendency to dislocation. The results are better in shortening the time of treatment and from the fact that when bony union is solid muscle function is just as good as before the injury. By the functional treatment, therefore, the result as to the union of bone should be just as good, while as to function of the muscles very much better than when immobilization has been the method employed. Time valuable to the patient is, therefore, saved. We have learned in abdominal surgery that it is not necessary to keep the patients in bed and at rest three weeks or more, when the peritoneal cavity has been exposed by a muscle-splitting operation and the wound accurately closed with layer suture. Many surgeons, overweighted by traditional conservatism, still waste precious time of their laparotomized patients. The same is true of fractures. The injured limb should be allowed as much motion as is compatible with the fixation of the fragments. Dressings should be frequently changed, passive motion and massage employed at frequent intervals, and, in certain cases, other means for the improvement of function, like Bier's hyperemia and electricity, resorted to; in any possibility of delayed callus formation—drugs like thyroid extract, specific treatment in syphilitic patients, tonics and fresh air in debilitated patients.

Deutschländer<sup>1</sup> and Bowser<sup>2</sup> in their contributions discuss the details of functional treatment and demonstrate how more frequently it can be employed. Klapp<sup>3</sup> has devised a special motor-driven apparatus with which massage by means of a strong current of hot or cold air can be given, and, in addition, hyperemia produced. This method of Klapp would make the functional treatment of fractures in the out-patient department and in the ward simpler and less time-consuming.

<sup>1</sup> *Zentralbl. f. Chir.*, 1906, xxxiii, p. 1305.

<sup>2</sup> *British Medical Journal*, October 27, 1906.

<sup>3</sup> *Zentralbl. f. Chir.*, 1907, xxxiv, p. 454.

These three articles well demonstrate the change in our methods of treating fractures and confirm the pioneer Lucas-Championnière, who for many years has apparently preached in the desert.

Sommer<sup>1</sup> in a dissertation concludes that the function of the soft parts can be maintained without passive motion or massage by frequent faradization through openings in the fixation dressing or through electrodes previously embedded. I am not prepared to venture an opinion at this time, but it appeals to me as a very important method of treatment in those cases of fracture in which the tendency to dislocation requires a more or less continuous fixation bandage, and makes early passive motion and massage a dangerous procedure, except in the most experienced hands.

**Callus Formation.** Sommer<sup>2</sup> based his new method of after-treatment on careful x-ray studies of callus formation in recent fractures. He demonstrated that in impacted fracture, and in all fractures with good apposition of the fragments, callus formation was least. Excessive formation of callus, as a rule, indicates displacement of the fragments, comminution or interposition of soft parts. That is, the callus, as a rule, is proportionate to the difficulty of filling the gap between the fragments. There are, of course, some exceptions to this rule. Children and certain individuals throw out more callus in proportion to the bone injury. Callus formation in the bones of the lower extremity, especially the small pipe bones of the foot, is greater than that in the upper extremity. Sommer does not explain this, except by the statement that the burdening of the lower extremity is greater. Perhaps in the lower extremity there is more passive hyperemia than in the upper.

**Passive Hyperemia in the Treatment of Fractures.** The name of Bier has become associated with this method of treatment in all conditions, but John B. Roberts<sup>3</sup> stated before the American Surgical Association in May, 1907, that he had employed passive hyperemia by means of a rubber bandage about the limb for delayed union in fractures eleven years ago, and published it in 1898. At that time he was not familiar with Helferich's publication in 1887. Apparently both antedated Bier, and Roberts deserves the credit for introducing it first in this country. Bier was using hyperemia in 1892, when I visited von Esmarch's clinic in Kiel, but I saw no examples of fracture.

Deutschländer<sup>4</sup> writes enthusiastically on the subject of obstructive hyperemia in fractures, and gives in detail an example of osteotomy for osteomalacia in a child of ten in which the healing, apparently, was hastened by this treatment. Obstructive hyperemia is not necessary in the routine treatment of fractures. It is an agent which should be employed in the event of delayed union. Its application is simple and painless.

<sup>1</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 685.

<sup>2</sup> Loc. cit.

<sup>3</sup> Surgery, Gynecology, and Obstetrics, July, 1907, v, p. 16.

<sup>4</sup> Zentralbl. f. Chir., 1906, xxxiii, p. 337.

**Pseudarthroses.** I have referred to Bier's<sup>1</sup> suggestion to inject fresh blood into the region of the fracture if there is delayed union. Hildebrand<sup>2</sup> disagrees with Bier. He is of the opinion that there is no evidence to prove that blood in the region of the periosteum and bone aids the periosteum in bone formation; nor is there any evidence that such free blood can give nourishment to the periosteal or endosteal osteoblasts. And in his experience with one case of pseudarthrosis he obtained no result from the injection of fresh blood. On the other hand, Jotchkowitz<sup>3</sup> prefers the injection of tincture of iodine, and reports two successful cases.

The subject of delayed and non-union of fractures with pseudarthrosis is by no means a settled one, and it is difficult to estimate the efficacy of the various therapeutic measures. In the majority of fractures treated in the recent state union will take place if the fragments are in apposition. When delayed or non-union is observed between fragments in proper apposition the surgeon should exhaust all non-operative measures before resorting to resection. Theoretically, there is no reason why the freshened ends should unite any more rapidly than the previous fracture, and practical experience has confirmed this. In these cases ambulatory treatment, massage, passive motion, hyperemia, injections of fresh blood and irritants, fresh air and tonics, thyroid extract should all be employed.

If the fragments are not in apposition and there is non-union, operation should first be employed.

The absolute apposition of fragments is not always necessary for union. In a recent observation of my own, of a fracture of both bones of the forearm, a few centimeters above the wrist in a boy of ten, I was unable to replace the lower end of the radius; the ulnar fragments were in place. On two occasions under ether attempts were made, but each time the *x*-rays showed the little fragment of the lower end of the radius was still dislocated *ad latum* (Fig. 3).

On account of the shortness of the lower fragment I felt that operative reduction would be difficult and was of the opinion that healing would take place without shortening or deformity if extension was maintained. This has taken place. The periosteum, apparently, has not been torn on one side, and here there has been almost a reproduction of the lower end of the radius; there is no shortening and no deformity.

Figs. 4 and 5 are good illustrations of the possibility of solid bony union with considerable overlapping of fragments.

I do not wish to be understood that every attempt should not be made to obtain anatomical reduction of the fragments, but in some cases in which this is not possible without operation a careful study of the case in the light of recent experience will allow the surgeon, in a few instances,

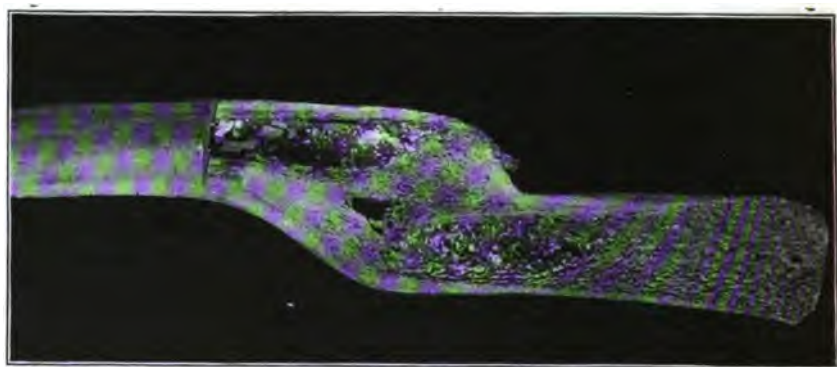
<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906.

<sup>2</sup> Zentralbl. f. Chir., 1906, xxxiii, p. 345.

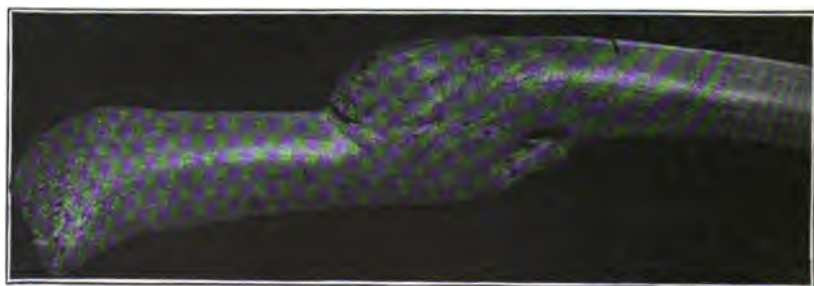
<sup>3</sup> Ibid., p. 602.



**FIG. 3**



**FIG. 4**



**FIG. 5**



to choose conservative treatment—that is, incomplete reduction is not always, of itself, an indication for operation.

In cases of pseudarthrosis associated with faulty position of the fragments or interposition of soft parts, good results can be expected from operative measures. The operation, however, should not be delayed, because the bone in the end of the fragments either atrophies or becomes eburnated, and the longer the delay the greater the length of the bone to be resected.

Coenen<sup>1</sup> reports on the methods and results of plastic operations for pseudarthroses.

**Operative Treatment of Fracture.** Recent literature seems to show a tendency to conservatism rather than to the operative treatment of fracture in the recent state. Ranzi,<sup>2</sup> from the surgical clinic of von Eiselsberg in Vienna, reports 50 operations in which the fracture was fresh in but 3 (6 per cent.)—2 in the humerus and 1 in the femur. In the remaining cases the fracture was old, with bad position of the fragments, with or without union. Undoubtedly, in many of the cases of pseudarthrosis or bad union, proper reduction in the recent state would have accomplished a perfect cure; in a few operations in the recent state, because of inability to reduce the fragment, was indicated. This contribution from a large clinic demonstrates that fractures can be properly treated without operation if seen early after the injury.

Ranzi, in summarizing, is of the opinion that fractures of the shaft of the long pipe bones, as a rule, can be treated by conservative means and good functional results obtained, even when the x-rays show imperfect reduction. In epiphyseal fractures operation is indicated if perfect reduction cannot be obtained, because the change in the anatomical position of the fragments influences growth. Fractures at the elbow-joint, and especially of the condyles of the femur, are better treated by operative reduction and wiring. Supracondylar fractures, as a rule, can be reduced without operation. Fractures of the upper end of the humerus give good results with extension. When the fracture is associated with dislocation of a fragment including a portion of the head, open incision should be employed if perfect reduction cannot be made, but not infrequently the dislocated fragment can be forced into position. In my experience, this is best accomplished in extreme abduction. Fractures of the olecranon and the patella should always be subjected to immediate incision and suture. Fractures of the neck of the femur will be discussed in detail farther on. Ranzi inclines, therefore, to the conservative treatment of recent fractures. I think he exaggerates the danger of infection. In my opinion, the argument against immediate operation in recent fracture is

<sup>1</sup> Archiv f. klin. Chir., 1907, lxxxiii, p. 1011.

<sup>2</sup> Ibid., 1906, lxxx, pp. 567 and 843.

not the danger of infection, but that the operation is not absolutely necessary, except in selected cases. The cases of pseudarthroses and badly united fractures admitted to surgical clinics, as I have stated before, are, in the majority of instances, due to improper treatment in the recent state. The physician who treated these patients was surely less competent to operate than to follow conservative means, and the fact that I wish to emphasize to the general practitioners is, that if they employ the *x*-rays and ether for reduction, they can train themselves to treat with success the majority of fractures. It is the surgeons connected with large clinics with accumulated experience in the treatment of fractures who should point out to the general practitioner those cases in which operation is indicated, and this I have attempted to do in the pages of this periodical from year to year. I am of the opinion that the greatest good can be done to the greatest number at the present time by improvement in the conservative treatment of fractures. The operative group is a small one; it requires expert opinion to select the cases, and a trained surgeon to operate upon them.

Ranzi emphasizes the point, already alluded to, that when there is delay or faulty union from bad position the indicated operation should not be put off. The longer the interval the greater the difficulty in the operative technique, and the less the probability of a successful result.

Schlange,<sup>1</sup> in his discussion of the operative treatment of irreducible dislocations and fractures, takes a more radical view. As to dislocations, there can be no question—every irreducible dislocation should be subjected to immediate open incision and reduction. But, as a matter of fact, the number of cases is small. The ordinary dislocation is not difficult to reduce in the recent state. If one employs the proper manipulations under anesthesia and fails to reduce the dislocation he will find in the *x*-rays a fragment of bone or, at the operation, interposition of soft parts to explain his failure. The time to operate is at once. The changes that will take place in the joint and its surroundings by delay may be irreparable.

There should be no old dislocations.

Schlange believes in getting both an anatomical and functional result. Theoretically this is correct, but practically, as I have stated before, there are certain cases in which the anatomical result is not essential. I agree with Schlange and others that the dangers of subjecting a recent fracture to operation are not great. It is an interesting field of surgery, but the operation should be done under the best surgical environments; the periosteum should always be preserved and the surgeon must not enter this field without unusual anatomical knowledge and perfect surgical technique. The reduction after an open incision is not always simple;

<sup>1</sup> Archiv f. klin. Chir., 1907, lxxxi, part ii, p. 9.

approximation and wiring are frequently difficult, and, it must be remembered, not always necessary; special instruments are required. The Gigli wire-saw in the majority of cases is the best means for removing bone. In the recent state this should be avoided if possible; in older fractures it is always necessary.

I will discuss the indications for operation again under special fractures, but I wish to repeat, with emphasis, the view already expressed, that in this country it is more important to improve our methods of conservative treatment before enlarging the field of operative indications. When operation is done, the most important point of all is the preservation of the periosteum.

Martin's<sup>1</sup> contribution, which I mentioned last year as presented to the American Surgical Association, has been published with excellent illustrations.

**Compound Fractures.** Rimann<sup>2</sup> presents a most excellent study of 238 cases of compound fracture from Trendelenburg's clinic in Leipzig. The principle of treatment throughout has been conservative, and in each case an attempt has been made to close the wound and thus to transform an open into a subcutaneous fracture. Drainage is only employed when the nature of the soft-part injury demands it.

In the majority of their cases the patients were seen shortly after the injury. The skin of the injured extremity is cleansed with soap and water and shaved; this is followed by alcohol, ether, and bichloride—that is, the disinfection of the skin follows the ordinary methods of preparation for any clean operation. Rimann emphasizes the importance of protecting the wound or wounds during the skin cleansing.

The wound is now inspected by holding it apart with mouse-tooth forceps and sponged with aseptic gauze. No attempt is made to disinfect the subcutaneous wound, except when it is contaminated with visible dirt. In such instances, cleansing is done with sterile water or salt solution. The extent of further investigation or operative intervention varies with the injury of the soft parts and the comminution of the bone. Cavities filled with blood, and hematomas, are incised and wiped out; cavities due to tearing are opened and cleansed; projecting pieces of bone are removed when they cannot be reduced, and loose bone denuded of its periosteal attachments is also removed. Rarely is suture of the fragments performed. An anesthetic is given if necessary, and the fracture is reduced as it would be in a non-compound injury. In simpler cases the skin wound or any exploratory incision is closed. If there has been much laceration of soft parts, hematoma or tear pockets, drainage with small pieces of rubber tissue is employed between the sutures. The limb is then dressed in a fixation bandage according to the nature of the frac-

<sup>1</sup> Surgery, Gynecology, and Obstetrics, August, 1906, iii, p. 258.

<sup>2</sup> Beiträge z. klin. Chir., 1906, I, p. 531.

ture; plaster with windowing over the wound is preferred. When there are no symptoms of infection the drainage is removed in a few days. In the event of symptoms of infection, local and general, the wounds are opened for more frequent dressings.

When the traumatic wound cannot be approximated, Trendelenburg always attempts closure by means of skin and subcutaneous-tissue flaps from the surrounding healthy soft parts. The flaps are fashioned according to the indications, the most important point being the preservation of the blood supply.

Rimann looks upon this method of treatment as the most conservative. Its chief object is to obtain, if possible, a closed soft-part wound with rapid healing, so that the fracture will heal subcutaneously. The results apparently are excellent. In addition, they always employ a prophylactic injection of antitoxin of tetanus.

Ochsner<sup>1</sup> is an advocate of the open-wound method. As regards disinfection he follows the method just described. On the whole he favors, in addition, antiseptic disinfection of the soft-part wound and fracture, but he does not close the wound with suture.

The subject of compound fracture was discussed in detail in 1905,<sup>2</sup> using Klauber's contribution from Wölfler's clinic in Prag. This author demonstrated that the consensus of authority favored conservatism in the treatment of compound fractures, and I called attention to the fact that we have returned to the principle first employed by Lister, except that we have forgotten his use of pure carbolic acid. I agree with the conservative treatment of compound fractures and with Klauber and Rimann. The description just given of methods employed by Rimann represents on the whole the best. Given a compound fracture, the first question to be answered is: Is amputation indicated? The best time to amputate is in the recent state, but this should only be resorted to when the local conditions are such that there is no doubt that the limb cannot be saved. The next question is: How much should be done? Other things being equal, the less operative interference, the better. Large hematomas and tear pockets should be opened and cleansed; visible contamination must be washed out; spicules of bone denuded of periosteum are to be removed, because they will act as foreign bodies; loose pieces of bone, however, with sufficient periosteal attachments to ensure their life, should remain. On general principles, fixation of the fragments is contra-indicated, because it requires further manipulation, and, even though carefully performed, there is the risk of periosteal detachment. The greater the injury of the soft parts, the greater the danger of bone suture. When the soft-part wound is simple, bone suture may be employed if the nature

<sup>1</sup> Reprint from *Medicine*, E. G. Swift, 1906.

<sup>2</sup> *PROGRESSIVE MEDICINE*, December, 1905, p. 190

of the fracture indicates it. Experience has demonstrated that the chief fault in the treatment of compound fracture is unnecessary and prolonged manipulation with the object of replacing and wiring fragments. In a compound fracture the paramount objects in view are the proper cleansing and draining of soft-part injuries.

Before the days of Lister wide-open wounds or amputation were the rule. No one could have been more conservative than Lister, who simply disinfected and protected with carbolic acid; yet he revolutionized not only the treatment of compound fracture, but all surgery.

Surgeons emboldened by the armamentarium of antiseptic surgery increased operative intervention for compound fracture, which reached its height in von Volkmann's brilliant results in 1887, by his operation termed *débridement*. Since then, the pendulum has swung back to the conservatism of Lister, first, because the results were just as good in all cases, and much better in some. In the hands of other surgeons von Volkmann's brilliant results have not been obtained.

When surgeons follow the conservative methods just described and observe severe wound infection in a certain number of cases, it is not the fault of the method, but due to the infection of the wound at the time of the injury. Every compound fracture is an infected wound. In the majority of cases the organisms which come from the clothing and skin of the injured patient, or from foreign dirt introduced, are few in number, not virulent, and, if the wound is properly treated and there is good circulation, the tissues will take care of these organisms. However, if virulent organisms have gotten into the wound, clinical and experimental investigation shows that no amount of cleansing or disinfection will ensure against wound infection. This is especially true of tetanus, virulent streptococci, and gas bacilli.

In PROGRESSIVE MEDICINE, December, 1899, I reported cases of compound fracture (p. 158) in which emphysematous cellulitis due to the gas bacillus of Welch took place in wounds seen early and properly treated. The possibility of this rare and accidental virulent infection of compound fracture must be borne in mind. The longer the interval between the injury and the first treatment, the greater the danger of infection. This element of time should influence the surgeon in the closure of wounds and drainage. Evidence of contamination of the wound other than from the skin of the patient and his clothing increases the possibility of an introduction of more virulent organisms. This evidence must also influence treatment. The two factors—time and contamination—of themselves should be considered, even though the wound be small and the circulation of the soft parts good. On the other hand, the most important factor in the resistance to infection is the circulation of the soft parts about the fracture. It is quite possible to have

a small skin tear and a large hematoma and tear pockets which do not communicate with the open wound. Here we can exclude primary contamination of the hematoma and pocket. When the skin defect communicates with the subcutaneous lacerated tissue the possibility of infection is present.

The prophylactic treatment for infection of the soft-part wound is not so much primary disinfection as open wound and drainage. Rimanni can be criticised in his first statement that in compound fracture the object is, if possible, to close the wound. Yet, when we come to read his description in detail, we find, as a matter of fact, that this ideal method is only employed in suitable cases and that drainage is instituted when indicated. Ochsner, on the other hand, can be criticised for advocating open-wound and drainage as a routine procedure. The danger of infection in compound fracture, both of the soft parts and bone, is exaggerated. When these cases are seen early after the injury, splendid results are obtained by simple methods. It is the object and art of progressive surgery to be able to select the few cases which cannot be treated by routine procedures.

In my own experience I would advise the employment of pure carbolic acid as a method of disinfection in the primary treatment of the wound, and suggest, to those whose experience is yet comparatively limited, to employ drainage and a partially open wound in all doubtful cases. I would also urgently warn against unnecessary manipulation and wiring of the fracture in all compound injuries, and especially when the period of time between the injury and the first dressing is more than a few hours, and when there is extensive soft-part laceration.

**Mechanism of Fractures.** From the scientific standpoint the relation of the etiological factors to the form of fracture is of interest, but, as a matter of fact, of little aid in diagnosis. It is always difficult and often-times impossible to estimate the direction and number of forces which have produced the fracture. This is illustrated by the recent communications of Müller,<sup>1</sup> Zuppinger,<sup>2</sup> and Kroh.<sup>3</sup>

Müller, from his x-ray studies of fracture in von Brunns' clinic, finds that bending force predominates, but the lines of fracture are not always the same. He also was able to demonstrate fractures due to the forces of torsion and crushing and proved that by torsion the line of fracture may be transverse, spiral, splintered, or longitudinal. As a rule, in bending fracture the lines are quite similar, but he was unable in his group of cases to find any examples of Zuppinger's strain or "scissor" fracture (*Abscheerungsfractur*). Zuppinger, in reply, is of the opinion that Müller has overlooked examples of fractures by these forces. I quote these two communications to demonstrate that among surgeons giving

<sup>1</sup> Beiträge zur klin. Chir., 1906, I, p. 297.

<sup>2</sup> Ibid., lii, p. 301.

<sup>3</sup> Deutsche f. Chir., 1907, lxxxvi, p. 281

special attention to the character of the force or forces and their relation to the line of fracture there is considerable difference of opinion. Kroh's communication is based on an experimental study and concludes that pure torsion produces a fracture of spiral form only in bones the seat of some pathological process. In normal bones there must be another factor besides torsion to produce this fracture.

**Glycosuria after Fracture.** Konjetzny,<sup>1</sup> in studying the urine in 19 cases, demonstrated glycosuria in 68 per cent. It is seldom present after the fourth day, in a few cases up to the second week. If there is a second trauma—to reduce the fracture or an operation—the glycosuria reappears. He is of the opinion that it is due to fat emboli in the medulla oblongata. The relation of this traumatic glycosuria to diabetes, if present at all, could not be demonstrated in his cases. This observation is of interest, because, if one examines the urine of a recent case of fracture previous to a contemplated operation, the presence of glycosuria need not be looked upon as a contra-indication.

**Spontaneous Fractures in Paralysis.** Eckel<sup>2</sup> reports 3 cases in patients suffering with paralysis. In one the patient was in an extreme degree of marasmus and the fractured tibia showed evidence of marked osteoporosis: The other two patients were in good nutritive condition, but at the autopsy in 1 with multiple fractures the bones were the seat of marked osteoporosis, and there was excessive callus formation at the site of the fractures. Eckel is of the opinion that the bone changes are due to lesions of the spinal marrow and that in the future, at autopsy, all the bones should be examined and the changes studied in their relation to the segment of the cord involved.

In *PROGRESSIVE MEDICINE*, December, 1905 (p. 230), the entire subject of pathological fractures was fully discussed and the difference of opinion in regard to the etiological relation between lesions of the brain and of the spinal cord to bone mentioned.

**X-rays in Fractures.** Max von Brunn<sup>3</sup> calls attention to the well-known fact that in every case of fracture two views should be taken. He gives the x-ray studies of four fractures in which the anteroposterior views of the bones of the leg show a fine line of fracture which might be looked upon and diagnosticated as subperiosteal or fissures. Yet, in the lateral view there is dislocation of fragments. He is of the opinion that in every case of fracture there should be at least two views.

**Injury of Vessels in Fracture.** In *PROGRESSIVE MEDICINE*, December, 1899, I discussed in detail traumatic gangrene due to rupture of the inner arterial coat and its possibility in association with a fracture, especially when the limb is caught between two opposing forces. Since that time there has been very little literature on this subject. Von Brunn<sup>4</sup>

<sup>1</sup> Zentralbl. f. Chir., 1906, xxxiii, p. 441.

<sup>2</sup> Ibid.

<sup>3</sup> Beiträge zur klin. Chir., 1906, I, p. 77.

<sup>4</sup> Ibid., 1907, lii, p. 594.

again calls attention to vessel injury due to fracture and gives the literature to date. The communication, however, adds nothing, except further cases, to the statement made in this journal in 1899. This lesion is now of greater interest, because of the advances in surgery of the vascular system. When there is evidence of arterial injury one should cut down upon the artery, open it, turn out the blood clot, resect the portion the seat of rupture, and do an end-to-end anastomosis. If the length of the injured portion of the artery is too great for anastomosis an attempt to reestablish circulation in the limb should be made by arteriovenous anastomosis. I will discuss this more in detail under Surgery of the Vascular System. Torrence,<sup>1</sup> of Birmingham, reports a case of compound fracture of the leg in which he did an anastomosis between the saphenous vein and anterior tibial artery. In this case both vessels were torn. Apparently the anastomosis maintained circulation for at least two weeks, and the gangrene was limited to the foot. The incomplete success was not due to the suture, but the extensive soft-part injury. In cases in which the artery is simply contused, with rupture of the inner coats and the formation of a thrombus, resection and end-to-end anastomosis of the injured artery should give successful results and save the limb.

**OBSTRUCTION OF THE ARTERY BY COMPRESSION OR KINKING.** Mage-nau<sup>2</sup> reports an injury with which I was not familiar—one which produces complete arterial obstruction and if not relieved may lead to gangrene. In his case there was a fracture of the lower epiphysis of the humerus; the soft parts were caught between the dislocated fragments and these pulled on the brachial artery and produced a kink. Clinically there was no radial pulse, a cold forearm, and paresthesia. This was sufficient evidence to indicate arterial obstruction. The brachial artery was exposed at the seat of fracture and its kinking demonstrated. Reduction of the fracture with relief of the soft parts caught between the ends relieved the kink and restored circulation of the forearm. In the literature only a single similar case was found. In this instance it was not recognized clinically, nor was there any attempt to expose the artery. At the shoulder-joint amputation on the eighth day for gangrene above the elbow, it was found that the brachial artery was not contused or ruptured, but caught and obstructed in the fork end of the lower fragment of the surgical neck of the humerus.

In simple and compound fracture with evidence of obstructed circulation immediate exposure of the artery near the seat of fracture is indicated. There may be a rupture with a hematoma, a rupture with thrombosis without hematoma, a rupture of the inner coats with thrombosis, or a kinking of the artery without rupture or injury. The latter is easily remedied; the others demand some form of arterial or arteriovenous suture.

<sup>1</sup> *Annals of Surgery*, September, 1907, vol. xlii, p. 333.

<sup>2</sup> *Beiträge zur klin. Chir.*, 1907, lii, p. 590.



**Fractures of the Pelvis.** As it is impossible within this short space to properly discuss, I shall only refer to Ludloff's splendid monograph<sup>1</sup> on vertical and oblique fractures of the os sacrum near the sacro-iliac synchondrosis. He also refers to fractures of the processes and joints of the vertebræ. The important facts which he brings out are that the clinical symptoms are obscure, that the lesion is quite common and is usually overlooked, and that the patients are frequently considered malingersers, especially if they have accident insurance. In patients with the history of an injury followed by pain, neuralgia, areas of anesthesia, loss of muscle power, and slight spinal curvatures, careful x-ray studies should be made and this splendid monograph of Ludloff consulted. This contribution is another example of the progress made by orthopedic surgeons, who devote time and energy to the investigation of apparently obscure lesions neglected by the general surgeon. The explanation for pain in the region of the spinal column is a subject for investigation, and orthopedic surgeons have added much to the diagnosis and treatment.

Liebold<sup>2</sup> reports a case of spontaneous fracture of the os ischii in tabes. It was associated with excessive callus formation and osteophytes at the site of fracture without involvement of the hip-joint—a different pathological picture from a simple fracture without lesion of the spinal cord.

**Fractures of the Neck of the Femur and Coxa Vara.** Among all fractures those in the region of the head and the neck of the femur present problems which are by no means settled. The results of treatment in the recent state, of union with deformity (coxa vara traumatica) and of pseudarthrosis are by no means satisfactory. The literature of this subject was first discussed in *PROGRESSIVE MEDICINE*, December, 1899. In that contribution, as coxa vara was a subject of comparatively recent development, I discussed the literature from its beginning. Since this date I have attempted to critically review all the more important contributions. There are three problems: (1) The treatment of the injury in its recent state, (2) the correction of the deformity (coxa vara traumatica) in old cases, and (3) the treatment of the ununited fracture of the neck of the femur (pseudarthrosis).

In spite of the claims of Bardenheuer, treatment by extension for fracture of the neck of the femur does not yield, at least in this country, uniformly satisfactory results. I have mentioned Whitman's method of fixation of both lower limbs in marked abduction. At the present time, with my limited experience, I am of the opinion that it is the method of choice. No contributions have appeared either in foreign or English literature to indicate that Whitman's method has been extensively employed. I have been informed by a personal communication that this method has proved very satisfactory in the Bellevue Hospital. The only perfect anatomical and functional results which I have ever obtained in

<sup>1</sup> Beiträge zur klin. Chir., 1907, liii, p. 161.

<sup>2</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 86.

fracture of the neck of the femur were accomplished by Whitman's abduction treatment. In *PROGRESSIVE MEDICINE*, December, 1905, Whitman's method was discussed and illustrated. The original communication was read before the New York Academy of Medicine in April, 1905, and is fully illustrated in the published report.<sup>1</sup> I refer the readers to this article for the details of treatment. Fig. 6 shows the method of reducing the deformity and the position of the patient in which the plaster is applied.

In March, 1906, the subject was again presented before the Johns Hopkins Hospital Medical Society.<sup>2</sup>

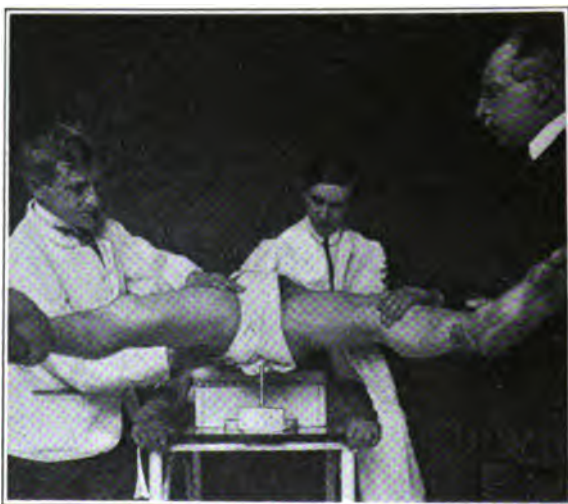


FIG. 6

In extreme abduction the trochanter of the non-injured limb is forced against the pelvis and fixes it. Now, when the injured limb is extended and abducted its trochanter comes against the pelvis, forces the distal fragment into position with the proximal fragment. In my first experience with this method, the patient was a male, aged sixty-five years: there was a history of a fall on the right hip; I saw him a few hours after the injury. The affected limb was rotated out, adducted, and there was apparent shortening. Measurements demonstrated absolute shortening between the trochanter and the anterior iliac spine—the clinical picture of fracture of the neck of the femur. The next day the patient was anesthetized with ether and placed in the position shown in the illustration from Whitman. First, an assistant abducted the non-affected limb to the extreme limit; two assistants held the shoulders; now a fourth assistant slowly extended and abducted the injured limb, while the operator placed

<sup>1</sup> *American Journal of Medical Sciences*, July, 1905.

<sup>2</sup> *Therapeutic Gazette*, May, 15, 1906.

the left hand grasping the inner surface of the thigh near the perineum and with the right hand pushed down on the trochanter. When abduction was complete the measurements of the limbs were equal. Measurement made before, with the limbs in straight position, showed shortening. Instead of fixing both extremities and the body in plaster I applied from axilla to external malleolus an external lateral wire splint on both sides. These splints were first fixed with adhesive straps; they were well padded with blankets. A few turns of plaster bandage were made over the chest in the nipple line, over the abdomen covering the trochanter and anterior iliac spines, the upper portion of the thigh, and above the knee. The only advantage that this has over plaster is that it is lighter, apparently more comfortable, allows openings for bathing and rubbing, and is more easily and quickly changed (Fig. 7).



FIG. 7

Three days later Dr. Baetjer took an *x*-ray. There was an oblique fracture in the neck of the femur near the trochanter, not between the head and neck. The fragments were in perfect position. The line of fracture can just be distinguished in the *x*-ray. This dressing was changed in two weeks without anesthesia, the patient was bathed and rubbed, and the dressing replaced with less plaster. It was now changed once a week for five weeks. The abducted position was constantly maintained; the change of dressing with bathing and massage gave great comfort; it could be done more frequently if necessary; each dressing requires from one hour to an hour and one-half, and one needs at least four assistants. The patient is lifted on an operating table with the footboard

down; the pelvis is at the edge of the table; the dressings are removed; then the patient is bathed and rubbed; now he is lifted, with a block under the sacrum and shoulders, and the splints readjusted; the long wire splints should be heavily padded with blankets; after the second week the wire splint on the non-affected side is stopped at the knee; this allows the patient to flex the leg. After the fifth week all dressings were removed, but the abduction was maintained in bed by bandaging. At the end of the seventh week the patient was allowed to get up on crutches, but he did not bear weight on the affected limb for three weeks longer. The abducted position, therefore, was maintained for seven weeks and no weight was borne for ten weeks. When the fracture is nearer the head the time should be longer, at least three months. In this case the *x-ray* taken ten weeks after the injury shows no changes, and at the present time, five months after the injury, there is every evidence of a perfect result.

This is my first experience in which I have accomplished a perfect functional and anatomical result in a fracture of the neck of the femur.

I have mentioned before in *PROGRESSIVE MEDICINE* that examination of all cases of fracture of the neck of the femur treated in the surgical clinic of the Johns Hopkins Hospital by extension shows shortening and adduction, and among these cases there are a number who walk without pain or crutch, but all with a slight limp; others have to use a cane or crutch, and there were some examples of non-union. This is the experience of every surgical clinic, except Bardenheuer's, who, however, does not claim to obtain perfect anatomical results in all cases.

I have a second case in a woman of seventy, in whom the fracture is near the head; this will be published next year, as it is but three weeks since the injury. In this case the shortening was greater, but when the patient was placed in the abducted position both limbs measured alike.

These two patients treated by Whitman's method were more comfortable than those treated by extension. The latter methods require hourly supervision; change in position is more difficult. When the patient is once fixed in the abducted position the surgeon need have no further anxiety; the position of the fragments will be maintained. In nursing such patients more help is required, because they must be bodily lifted, and constant change in position adds to their comfort. On account of the marked abduction of both limbs the care of the stools and the urine is simpler.

I trust surgeons in this country will try this method.

**HEALING OF FRACTURE OF THE NECK OF THE FEMUR.** While *x-ray* studies demonstrate that the abduction method of Whitman absolutely approximates the fragments in all cases, we yet cannot always be certain of bony union—that is, in this fracture perfect approximation of the fragments alone does not ensure solid bony union. There are two factors to be considered. The most important is the circulation of the bone. In old individuals suffering with senile osteoporosis callus production

may not be sufficient for the weight-bearing function. In all cases pieces of torn capsule may interpose between the fragments. The only argument for the immediate operative treatment for recent fracture of the neck of the femur is that the torn pieces of capsule can be removed and the capsule sutured. König is of the opinion that this suture of the torn capsule improves circulation and, therefore, the nutrition of the fragments and, *a priori*, ensures better production of osteoid tissue. From his clinic Frangenheim<sup>1</sup> has reported on studies of the healing process of fractures of the neck of the femur. Fractures at the head (*subcapital*) are less apt to show bony union than fractures at the base of the neck (*basal*)—that is, the nearer the fracture to the head of the femur the less the likelihood of bony union and the greater the probability of later static coxa vara. Frangenheim also calls attention to the interposition of torn pieces of capsule, but he apparently does not confirm König's statement that repair of the capsule greatly improves bony union, although he is of the opinion that if operation is performed the capsule should be sutured as well as the bone.

The point that I wish to emphasize is that if the fragments can be placed in perfect apposition by Whitman's abduction method, operation in the recent state, at least at the present time, should be postponed until we accumulate experience with this method. Theoretically, to operate and approximate the fragments by wire or nail should give no better bone approximation. It has only the advantage that it allows the removal of interposed soft parts and the suture of the capsule. At the present time experience with Whitman's method is not sufficient to demonstrate all its possibilities. In the past, I am quite confident, in the treatment of fractures of the neck of the femur perfect approximation of the fragments has not been accomplished by extension. If the x-rays show that abduction has not approximated the fragments, operation is indicated.

The next most important point in the treatment is the length of time which should elapse before the leg is allowed to bear weight. Schanz,<sup>2</sup> an orthopedic surgeon, demonstrates this. He calls attention to the fact that orthopedic surgeons frequently see the late results of fractures of the neck of the femur treated by the general surgeon, even though these patients have left their first treatment with an apparently good result. In a discussion at the recent German Surgical Congress the consensus of opinion among general surgeons was that the patient should be in bed at least three months. Schanz is of the opinion that this is not long enough, and he advises that these patients wear a splint which at first carries all of the weight of the body and, later, can be arranged to gradually transfer the burden to the femur. This splint should be worn at least a year. There is no doubt that in fractures of the neck of the femur

<sup>1</sup> Deutsche Zeitschr. f. Chir., 1906, lxxxiii, p. 401; Zentralbl. f. Chir., 1907, xxxiv, p. 74.

<sup>2</sup> Archiv f. klin. Chir., 1907, lxxxiii, p. 336.

which heal with shortening and adduction this deformity increases in a large proportion of cases until it gives rise to sufficient symptoms to be called *coxa vara traumatica*.

We have, however, not sufficient experience with perfect anatomical results to know whether the same danger is present. Surgeons, however, should bear this in mind and lengthen the treatment. I am of the opinion that it is not necessary to lengthen the time in bed. It seems to me that five or six weeks should be sufficient; then the patient should be allowed to get up on crutches. From now on one must choose between crutches or a special splint. If the anatomical position of a fracture is perfect I prefer, at least for the present, to try the crutches.

**OPERATIVE TREATMENT OF FRACTURES OF THE NECK OF THE FEMUR IN THE RECENT STATE.** In view of what has been said, it seems unnecessary to give much space to further discussion. In *PROGRESSIVE MEDICINE*, December, 1905, the entire subject was critically reviewed, especially emphasizing König's studies. It is not a very difficult operation to expose the fracture. However, the smaller the distal fragment (the head) the greater the difficulty of fixation.

**NON-UNION IN FRACTURES OF THE NECK OF THE FEMUR.** In properly treated cases this is observed only in older people and when the fracture is situated close beneath the head. At the present time we have no evidence that immediate operation will accomplish a cure; nor have I been able to find any cases treated by Whitman's method from which to draw conclusions. My most recent observation is of this character, and later I will be able to report on the results. At the present time I should advise Whitman's treatment. The head of the bone can be removed just as well at a later period if union is not accomplished, while if one attempts operation in the recent state by fixation a second operation may be necessary.

A woman, aged sixty years, quite frail, but active and in apparently good health, was properly treated by extension, but functionally there was no result. At my operation I found the shell of the head in the acetabular cavity; it seemed to have some circulation, but had thrown out absolutely no callus. Between the head and the trochanter there was a mass of scar tissue; the neck was completely atrophied; the head and this scar tissue were removed and the trochanter placed in the acetabular cavity, with the leg in abducted position.

Katzenberg<sup>1</sup> reports on two cases of pseudarthrosis after fracture of the neck of the femur in children, aged thirteen and fifteen, and concludes that the non-union was due to a pathological condition in the bone. The anatomical findings resembled the case just discussed. One patient was properly treated in the recent state by extension, the other not. Apparently this is a very rare result in children. As a rule, there is partial union

<sup>1</sup> *Archiv f. klin. Chir.*, 1907, lxxxii, p. 191.

with later coxa vara statica. This contribution also brings up the interesting point previously discussed, of the position of fracture of the neck in children. The majority of authorities are of the opinion that it usually takes place at the epiphysis. Whitman is of the contrary view. In one of Katzenberg's cases, at least, the fracture was not at the epiphysis. Apparently, Whitman is right to a certain extent, that fractures of the neck of the femur in children occur at some distance from the epiphysis in a fair proportion of cases. This communication of Katzenberg should be borne in mind from a medicolegal aspect, because here we have an example of an extremely bad result when proper methods were employed—a result not due to the treatment, but to a disease of bone.

**Coxa Vara.** Since my previous discussion of this subject recent literature has not added much. The traumatic origin of this deformity has been demonstrated more and more frequently, and cases of true coxa vara of Müller and Hofmeister are more and more rarely observed. The most recent classification by Elmslie<sup>1</sup> is as follows: (1) Congenital. (2) Infantile. (3) Adolescent. This is divided into acute traumatic, late traumatic, and the non-traumatic—the latter the true coxa vara adolescentium. (4) Associated with the diseases like rickets, osteitis deformans, and osteomalacia, and, I should add, bone cysts and osteitis fibrosa. (5) Secondary to acute and chronic bone inflammations—tuberculosis and pyogenic epiphysitis. (6) Osteo-arthritis. (7) Static—the late result of fracture of the neck of the femur.

This author agrees with the consensus of opinion that coxa vara is rare in rickets and is present in only the graver forms.

As to treatment, he emphasizes prevention. All injuries in the region of the hip-joint, especially in children, should be carefully examined by the x-rays and the affected limb not allowed to bear weight for some time, if there is any evidence of injury. In the acute stage in which, in addition to the deformity, there is pain and muscle-spasm, the patient should be put to bed at absolute rest in the abducted position, and when allowed to get up the hip-splint should be worn for some months. In the chronic stage, when the symptoms are due to the exaggerated deformity, subtrochanteric osteotomy is the method of choice. In regard to the latter advice my own experience demonstrates that chiselling and partial removal of the mushroom head has yielded most satisfactory results. Cuneiform osteotomy of the neck—an older method of treatment—has apparently been given up.

Schmidt<sup>2</sup> reports on the lesser injuries of the hip-joint which he calls contusion of the cartilaginous joint of the femoral head and its late complication—coxa vara. This is another investigation favoring the traumatic origin of many cases which come under observation with the

<sup>1</sup> Lancet, February 16, 1907; Zentralbl. f. Chir., 1907, xxxiv, p. 695.

<sup>2</sup> Mittheilungen a. d. Grenzgeb. d. Med. u. Chir., 1907, von Mikulicz's Supplement, p. 774.

typical symptoms without a history of injury, or many years after slight trauma.

**COXA VARA TUBERCULOSA.** This deformity of the neck of the femur associated with tuberculosis is relatively rare. Bally,<sup>1</sup> from Cönen's clinic, reports a case. The patient was a boy aged three years. The father had tuberculosis. The child was healthy up to eighteen months of age, when he began to complain of pain at night, especially when the left limb was moved. The acute symptoms subsided after fourteen days, but the child continued to walk with a limp and to drag the left leg. Some fifteen months later the acute symptoms reappeared after a traumatism, and the child was again unable to walk. The deformity consisted of flexion, adduction, and internal rotation, with real shortening between the anterior iliac spine and trochanter. The *x*-rays showed a coxa-vara deformity of the neck. The diagnosis lay between an epiphyseal separation from the recent trauma and tuberculosis which had been present since eighteen months of age in a latent form and was exaggerated by the recent trauma. The hip-joint was explored. There was tuberculous granulation tissue outside the capsule, tuberculous destruction of the acetabular cavity of a slight degree, and after resection of the head and neck a tuberculous focus was found in the latter. This case impresses me as one of interest: (1) To criticise the extensive resection of the upper end of the femur for a small tuberculous focus in a child of three years; (2) from the standpoint of differential diagnosis. The previous history of an acute coxitis at eighteen months with a latent period and recurrence of the symptoms after a slight trauma favors the diagnosis of tuberculosis, and in this case the leg was rotated in—a rare position for coxa vara. Bally<sup>2</sup> quotes Helbing as having reported 4 cases of tuberculous coxa vara from the clinic of Hoffa in Berlin. In Helbing's cases the patients were older and the tuberculous lesion was diagnosticated by the *x*-rays. This reference drew my attention to Helbing's article, which I had overlooked, and I find it one of the most comprehensive in recent literature. He reports all the cases of coxa vara from Hoffa's clinic and classifies them according to the etiological factors. His classification follows very closely that of Elmslie,<sup>3</sup> and I find that he adds to this, as I have already done, bone cysts and osteitis fibrosa. There are excellent *x*-ray pictures of the different types and some very beautiful pathological specimens. One which I reproduce (Fig. 8) is a perfect example of epiphyseal separation in the young—coxa vara traumatica.

Helbing in discussing the therapy takes practically the same views as Elmslie. He would agree with my criticism that in Bally's case resection was not indicated; conservative treatment should at least have been employed first.

<sup>1</sup> Archiv f. klin. Chir., 1907, lxxxiii, p. 648.

<sup>2</sup> Zeitschr. f. Orthop. Chir., 1906, xv, p. 502.

<sup>3</sup> Loc. cit.



The treatment is influenced by the etiological factor. As a rule, conservative measures should first be employed. Operation is indicated only in chronic cases with marked deformity, and here Hoffa prefers an oblique subtrochanteric osteotomy. In all the conservative measures, forced abduction, either in plaster or with passive motion and gymnastic, is the chief factor.

**Isolated Fracture of the Great Trochanter.** Krüger<sup>1</sup> in reporting a case discusses the literature. This fracture associated with fracture of the neck of the femur is not uncommon; isolated it is rare. It may be overlooked and diagnosticated contusion, because the patients often walk after the injury and later seek advice for deformity and pain. Both in the recent and later state the deformity is slight flexion, adduction, and inward rotation with no shortening, but a palpable trochanter nearer the



FIG. 8

anterior iliac spine than the other side. In the recent state swelling may prevent palpation of the fragment, and the diagnosis must rest upon the *x*-rays.

These cases should be treated: for slight dislocation of the fragment fixation in abduction and outward rotation; for greater dislocation operation and wiring. Both methods should be controlled with the *x*-rays. The photograph of the patient in Krüger's case resembles one illustrated by Thienhaus,<sup>2</sup> but the latter has reproduced the wrong *x*-ray, which, however, shows a very interesting epiphyseal separation of the lower end of the femur to be discussed later.

**Fractures of the Shaft of the Femur.** When the fracture is near the trochanter the flexion of the upper fragment is the most difficult to overcome. This may be met by traction of the limb in flexion. In children the right-angle-flexion position of the thigh with the leg in flexed position

<sup>1</sup> Deutsche Zeitschr. f. Chir., 1906, lxxxiii, p. 464.

<sup>2</sup> Annals of Surgery, May, 1906, xliii, p. 753.

undoubtedly meets the indications best. In adults there is an increasing tendency to operation in the recent stage. In fractures of the shaft of the femur, if the fragments can be approximated, traction with the thigh fixed in splints is the method of choice. In fractures of the shaft the chief danger to avoid is bending due to too early burdening. The limb may be straight with little or no shortening, but if the patient is allowed to walk the soft callus bends and angular deformities follow.

When the fracture of the shaft is below the upper third a plaster dressing with early ambulatory treatment gives excellent results. It is an expert method of treatment and should be checked with the *x*-rays. If the line of fracture is oblique or spiral, traction should be employed for at least three weeks before changing to plaster.

Bardenheuer's<sup>1</sup> book and his paper before the German Surgical Congress<sup>2</sup> outline his special methods of various forms of traction in fracture of the femur. The method is too complicated to discuss here, but every surgeon interested in the treatment of fracture should read these contributions. At the present time I am of the opinion that equally good results can be accomplished by simpler means; if not, I should prefer immediate operation. It seems impossible, in this country, to get the younger surgeons living in the hospital (internes) interested in non-operative methods of treatment. Bardenheuer's extension methods require constant supervision by one familiar with the method and also well versed in the principles of mechanics. In my own experience I have succeeded in getting equally good results with simple longitudinal extension. In cases in which this did not seem feasible, operation and wiring were employed with success. I would again emphasize the importance of employing some form of a splint—plaster is the simplest—to bear the weight of the body for some weeks after the patient is allowed to get up. In my early experiences, some of my best results were marred by later bending.

Fink<sup>3</sup> suggests a rather ingenious method of treatment for fracture of the femur. He fixes the thigh above the fracture and the pelvis in plaster up to the nipple, and then the lower fragment with the leg flexed at right angle at the knee in a second plaster cast. When these casts have hardened, he attempts to reduce the fracture with traction and manipulation, and then fills the gap with a third cast. This manipulation is repeated until the fragments are in perfect apposition. The treatment does not appeal to me. It is a pretty well accepted view that a fracture should be reduced, if possible, at once, especially if there be dislocation *ad longitudo-*

<sup>1</sup> Die Allgemeine Lehre von den Frakturen und Luxationen. Ferdinand Enke, Stuttgart, 1907.

<sup>2</sup> Archiv f. klin. Chir., 1907, vol. lxxxiii, p. 173.

<sup>3</sup> Zentralbl. f. Chir., 1907, xxxiv, Supplement, Nr. 31, p. 115.

and chiefly in the bones of the forearm, may be molded at later dressings.

Göcke<sup>1</sup> reports an interesting observation in which there was lengthening of the limb after healing of a fracture of the femur. As the fracture was oblique and the *x*-rays showed some overriding of the fragments there should have been at least 4 cm. shortening. He explains the lengthening by bone growth. Unfortunately this is rare. In this case it overcompensated the shortening due to overriding of the fragments.

**Epiphyseal Separation of the Lower End of the Femur.** This fracture, although rare, is one of considerable interest and of great importance, because if the epiphysis is not properly reduced there will be not only deformity, but impaired growth. The lower epiphysis is usually dislocated anteriorly and the upper fragment—the shaft—posteriorly. Compression or injury of arteries and nerves is not infrequent. Operation may be necessary for reduction. Luxembourg<sup>2</sup> reports a case of unusual interest, because the leg and lower epiphysis were dislocated outward. According to Poland, who in 1898, among 700 collected cases of epiphyseal separation, reports only 2 of this variety, it is rare. The diagnosis was not difficult in Luxembourg's case. The epiphysis could be palpated almost as a loose body to the outer side of the knee, and the lower end of the upper fragment to the inner side. Reduction was accomplished, and a satisfactory result obtained by Bardenheuer's extension.

**Fractures of the Patella.** Schäfer<sup>3</sup> reports on a simple method of suture employed in Witzel's clinic for a number of years with satisfactory results. Through a small skin incision above and below the patella two trocars are passed: one through the quadriceps tendon above, and the second through the patellar ligament below; the inner needle of the trocars is then removed and silver wires passed through the cannulas. These are then firmly tied over a gauze sponge placed on the patella approximating the fragments. The trocars should be curved with the concavity toward the patella. Plaster anterior splint for one week; change every week for massage; passive motion in the third week; wires removed in the fifth week, are the successive steps in the after-treatment.

Von Brunn<sup>4</sup> reports on an interesting investigation on what happens to the silver-wire suture when buried in the patella to approximate the fracture. He finds that in practically every case the wire has broken or pulled through the bone, and that bony union is rare in the *x*-ray picture of old cases. In a few instances the wire has slipped into the joint and become encapsulated. These patients complain of some pain and restriction of motion. The breaking of the wire apparently does not inter-

<sup>1</sup> Zentralbl. f. Chir., 1907, xxxiv, Supplement, Nr. 31, p. 113.

<sup>2</sup> Deutsche Zeitschr. f. Chir., 1907, lxxxix, p. 390.

<sup>3</sup> Zentralbl. f. Chir., 1907, vol. xxxiii, p. 704.

<sup>4</sup> Ibid., 1906, xxxiii, Supplement, No. 28, p. 123; Beiträge z. klin. Chir., 1906, vol. 1, p. 83.

fere with the functional result. Kausch<sup>1</sup> is of the opinion that if the silver suture is placed and fixed with the knee in slight flexion the silver suture will not be displaced, which he thinks is due to early passive motion.

While the majority of surgeons favor the operative treatment of this fracture, Lewisohn, from Czerny's<sup>2</sup> clinic in Heidelberg, claims that the conservatively treated cases not only compare favorably with those sutured, but even surpass them in the end results. In his method the blood effusion is removed by aspiration and pressure; the fragments are fixed by adhesive straps; massage is employed at once. He is of the opinion that bony union is by no means the most important factor.

Meyer<sup>3</sup> contributes a very interesting study of longitudinal fractures of the patella from Baer's clinic in Zurich. Apparently these fractures are not so infrequent. In the recent state they are usually seen by the general practitioner and, on account of the slight symptoms and loss of function, diagnosticated as sprains. They are seen by the special surgeon only later, because of chronic hydrops. Here, therefore, we have another etiological factor for intermittent joint hydrops.<sup>4</sup>

As the fracture is longitudinal, there is little displacement and, as the lateral capsule is not torn, very little loss of function. At the time of the injury the patients complain of local pain and sometimes claim to have heard a cracking noise. The secondary joint effusion is the prominent symptom. If such patients are seen early, before the marked joint effusion, the diagnosis of a longitudinal fracture can be made by flexing the knee; this separates the fragments. Meyer demonstrates that the usual anteroposterior or lateral view in the *x*-rays will not show the line of fracture, but one must take an oblique view from posterior-out to anterior-in, after displacing the patella outward, the leg in extension. In the recent state this fracture does not require suture; rest, fixation bandage for the effusion, and early passive motion and massage are sufficient; prolonged rest is contra-indicated, as in all joint injuries. When the original injury is overlooked there will be months, even up to a year, of recurrent attacks of joint effusion from slight injury or overexertion. This is due to the callus which projects into the joint cavity and impinges against the femur. Unless this possibility is borne in mind, the lesion might be mistaken for chronic arthritis and improperly treated. It is just this use that accomplishes a cure by wearing away the exuberant callus. Having demonstrated the fracture in the *x*-ray, the patient should be encouraged to use the limb, avoiding overexertion, and informed that after a time the symptoms will disappear. When there is a joint effusion the knee should have

<sup>1</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 530.

<sup>2</sup> Beiträge z. klin. Chir., 1906, lii, p. 196; review in Surgery, Gynecology, and Obstetrics, June, 1907, vol. iv, p. 793.

<sup>3</sup> Deutsch. Zeitschr. f. Chir., 1906, lxxxv, p. 656.

<sup>4</sup> PROGRESSIVE MEDICINE, December, 1902, p. 147.

rest for a few days and be supported later by adhesive straps. The contribution is of interest, as it brings out a simple etiological factor for recurrent joint hydrops.

My own experience with fracture of the patella, which began in Halsted's clinic in 1893, favors operative treatment. The results have been so uniformly good that, with the exception of a few cases of fracture without displacement, I have always operated in the recent state. Following the method of Halsted, the fragments have been approximated by suture of the torn capsule only with silk, care being taken to remove all torn soft parts between the fragments. As a rule, the operation has been performed a few days after the injury. In the recent state we have never found it necessary to wire the bone. During the last three years I have performed these operations under local cocaine anesthesia and have approximated the torn capsule with continuous catgut. In all of my cases I found tears, both internal and external, of the quadriceps tendon. The leg is fixed lightly in extension and adhesive straps; massage of the quadriceps muscle is begun at once; passive motion begins in the second week and is gradually increased; the patients are allowed to walk on crutches in the fifth week. Up to this time the flexion is restricted to 25 degrees. The skin wound is always closed with the Halsted subcutaneous suture of silver wire. Faulty union, even of the skin, has never been observed. The immediate results have always been good. Some years ago I looked up the ultimate results and found in every case perfect function. Apparently the fragments were in perfect apposition. No *x*-ray studies were made to demonstrate the character of the union. As during the same time, both in Halsted's clinic and in my own practice, an almost equal number of old, ununited fractures of the patella have been treated, we have evidence against uniform good results after the conservative treatment. Practically all of these cases had been treated properly in the recent state, if one looks upon the non-operative treatment as proper.

One patient was sent to me by Dr. Scott, of Hagerstown. He had an old fracture of the left patella with 6 cm. separation and had sustained a recent fracture of the right patella. He came under observation ten days after the last injury. This fracture had been treated with adhesive straps. The fragments were in such perfect approximation that I decided to give him the benefit of the doubt and operate on the old fracture first. When he began to flex this knee in bed, five weeks after the recent injury and before he began to walk, the fragments of the right patella separated, while the fragments of the sutured left patella held. The right side was then operated upon. There was fibrous union mixed with interposed torn capsule and torn capsule on each side of the patella.

The results of suture in the late stage with separation of the fragments do not give the uniformly good results observed after operation in the recent period. These depend upon the degree of separation of the frag-

ments and the condition of the quadriceps muscle. In such late cases the fragments have been approximated by wire suture which, however, do not perforate into the joint. The capsule on each side of the patella is also sutured. When the freshly sawn fragments cannot be approximated without tension, a plastic operation is performed upon the rectus muscle. In my case just mentioned, the rectus had to be cut through so that the horizontal incision became a diamond-shaped cavity, when the upper fragment was pulled down.

In these cases, as far as I have been able to ascertain, the sutured patella has not separated. Many of the patients have perfect function; a few, restriction of flexion. As we have never passed the silver wire into the joint von Brunn's experiences have not been duplicated. Now and then the wires have broken and worked through the skin.

The suggestion of Kausch<sup>1</sup> that the suture be made in flexion to about 30 degrees from full extension and the leg dressed for the first ten days in this position seems good. I have had no experience with this method. It is hardly necessary in recent cases, and in many of the older cases suture in this position would demand a more frequent plastic operation on the rectus. This is an operative manipulation which should not be resorted to unless absolutely necessary. I am unable to give positive statements as to bony union, except in one autopsy case some months after operation in which union was absolutely bony. I am of the opinion, however, that the most important point is suture of the torn tendon. The patella is sutured in older cases simply because the tendon is attenuated, and the best way to approximate the tendon over the patella is to bring the fragments of bone together. Lateral suture should never be neglected. Early massage of the quadriceps muscle and gentle passive motion of the joint are the most important factors to ensure subsequent joint function; drainage should never be employed. With careful technique there is no danger of infection. In the recent state it is a simple operation. When the fragments are multiple and the suture must pass through the joint, I should advise catgut rather than silver wire for suture.

E. J. Senn<sup>2</sup> recommends iodized catgut, and I am of the opinion that in the future, perhaps for all cases, catgut can be substituted for silver wire. The experience of von Brunn should at least suggest that catgut be given a trial.

**Internal Derangement of the Knee-joint.** When a traumatism to the knee does not result in a fracture or dislocation, the patient is by no means ensured against some immediate or permanent disturbance in which the ultimate loss of function may be greater than after the more easily recognized fracture or dislocation. König,<sup>3</sup> the master mind in injuries and diseases of the joints, brings this out in his most recent contribution in

<sup>1</sup> Loc. cit.

<sup>2</sup> Surgery, Gynecology, and Obstetrics, December, 1906, iii, p. 821.

<sup>3</sup> Deutsch. Zeitschr. f. Chir., 1907, lxxxviii, p. 337.

which he chiefly discusses injuries of the meniscus (semilunar cartilage). His conclusions are confirmed by Martina<sup>1</sup> in Graz. König writes that in German there is no appropriate word to describe these lesser anatomical injuries and for this reason he adopts the French term "derangement."

The lesser anatomical injuries of joints, exclusive of a fracture or dislocation, may be divided into two classes: injury of the soft parts which give rise to extrasynovial or intrasynovial lipoma, villous arthritis, or relaxation of the joint capsule or ligaments, and injuries of the cartilage which are followed by loose or pedunculated joint bodies. In all these lesions, if the irritation is kept up, further grave joint changes may take place and produce a condition which may be called traumatic arthritis deformans. Owing to its weight-bearing function and exposure, the knee-joint is the most common situation of all these possible lesions. In previous contributions to this journal I have given considerable space to the discussion of the literature of this subject. In 1899<sup>2</sup> I introduced the subject of free joint bodies, dislocation of the semilunar cartilage and joint lipoma. This was followed by<sup>3</sup> a discussion of the entire subject of traumatic arthritis. In *PROGRESSIVE MEDICINE* for December, 1906, some interesting communications on the regeneration of cartilage and on joint bodies were reviewed.

Added experience emphasizes the importance of again calling attention to the results of trauma to joints. All of these injuries, when recognized and properly treated in the recent state are rarely followed by the recurrent attacks of pain, joint effusion, and interference with function which are always the consequence in neglected cases. Fortunately, in the chronic cases subjected to operation before grave joint changes have taken place, the results are most satisfactory.

An injury to a joint, after the x-ray has excluded a dislocation or fracture, should not be treated lightly. For a few days, until the swelling has disappeared, the joint should have rest and massage; then for at least six weeks it should have some support; during this time the support should be changed at frequent intervals for massage and passive motion; imbricated, adhesive plaster is the best method of support. Among the numerous cases that I have treated in the recent state after this fashion I have yet to observe a single case of later derangement, while during the same period I have operated upon a number of cases of joint lipoma, villous arthritis, loose bodies, dislocated semilunar cartilage, chronic villous arthritis and, unfortunately, a few examples of grave traumatic arthritis deformans, in all of which there had been no proper treatment in the recent state.

Fortunately, as stated before, these operations in the late state relieve the patient of many of the symptoms, but in some cases fails to restore full joint function, especially for occupations in which there is overexertion.

<sup>1</sup> Deutsch. Zeitsch. f. Chir., 1907, lxxxviii, p. 369.

<sup>2</sup> *PROGRESSIVE MEDICINE*, December, 1899, p. 202-213.

<sup>3</sup> *Ibid.*, 1900, p. 162-172.

König and Martina demonstrate that in the recent state operation is not indicated for injuries of the meniscus, except in grave cases where it is completely torn and dislocated. On the other hand, practically all chronic cases should be subjected to operation. When the meniscus must be removed partially or completely, on account of its dislocation or contusion, the patient is relieved of the worst symptoms, and the joint is capable of ordinary function. König in 7 cases found that these patients complained of minor discomforts, especially inability to climb mountains, stairs, ladders, etc. This fact must be borne in mind in the prognosis. I doubt if a boy whose internal meniscus has been removed could play football. One of my patients could play tennis, but not as violently as before. Later, under the subject of Joints, I will call attention to the recognition and operative treatment of chronic, villous arthritis and joint lipoma, but I wish to emphasize here that patients suffering with recurrent attacks of joint pain and effusion, with or without locking, should be subjected to operation. Some anatomical defect will be found which can be repaired.

**Fracture of the Beak-shaped Process of the Tibia.** Since I first mentioned this subject, in 1903,<sup>1</sup> the literature has grown until Jensen, from the surgical clinic of Kraft, in Copenhagen, in reporting ten cases collects forty from the literature and gives forty-nine references. This contribution confirms what I<sup>2</sup> have already said. When the fracture is complete the symptoms are sufficiently grave to bring the patient to the immediate attention of the physician. The lesion may be mistaken for a fracture of the patella, a rupture of its ligament, or a fracture of the head of the tibia. The fragment may dislocate into the joint. In such cases, as a rule, open incision, reduction, and fixation are indicated. However, in many instances the fracture is incomplete, is looked upon as a sprain or contusion, and the patients seek advice later for a painful swelling in the region of the tubercle which has been incorrectly diagnosed tumor, bursitis, tuberculosis, pyogenic epiphysitis, or traumatic periostitis. An *x*-ray will immediately clear up the doubt. Jensen<sup>3</sup> has demonstrated that the tuberosity has its own bony nucleus which never appears before eleven years of age, and merges with the epiphysis at fifteen, and the epiphyseal line between the tuberosity and the epiphysis disappears between eighteen and twenty years of age.

This interesting lesion, which is very important from the standpoint of differential diagnosis, is not mentioned in recent text-books, and there is very little in American literature. Jensen claims that the injury is frequently found among football players.

Linkenheld<sup>4</sup> in reporting observations of a bilateral fracture of this

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1903, p. 145.

<sup>2</sup> Ibid., December, 1905, p. 233; and December, 1906, p. 201.

<sup>3</sup> Archiv. f. klin. Chir., 1907, lxxxiii, p. 30.

<sup>4</sup> Deutsch. Zeit. f. Chir., 1907, lxxvii, p. 226.



kind also gives the literature in detail. Both Jensen and Linkenheld refer to Key, in the *Lancet*, for 1827, as the author of the first report of a case of this injury.

**Fractures of the Upper End of the Tibia.** This is the first opportunity that I have had for presenting a collective study of fractures of this portion of the tibia. The only one which I have discussed is that situated in the tubercle or beak-shaped process, which relatively is one of the most frequent. Sonntag<sup>1</sup> collects all the observations from v. Brunns' clinic—thirteen cases in ten years, and all he could get from the literature. While fractures of the tibia rank, in frequency, next to those of the forearm, fractures of the upper third are the least frequent in this bone. Sonntag adopts Heydenreich's classification into fractures below the tubercle of the tibia and fractures of the joint end: the latter least common. Of fractures at the joint end there is epiphyseal separation, the isolated fracture of the tubercle or beak-shaped process, the isolated fracture of one or both condyles, and the compression fracture.

It is important to remember that the duration of healing of a fracture of the upper third below the tubercle is unusually long—on an average of three and a half months. It seems rather paradoxical, in view of Bier's statement on the stimulating effect of blood on callus formation, that delayed union in this instance is attributed to the marked blood effusion present in this form of fracture. Refracture is not infrequent. The line of solution of continuity is usually transverse or oblique, not infrequently comminuted, and there is one example of a longitudinal fracture. The fibula in the majority of cases is fractured with the tibia on the same plane and in the same line.

Traumatic separation of the upper epiphysis of the tibia is one of the rarest forms of epiphyseal injury. As a rule it is associated with marked joint effusion. The isolated fractures of the condyles are also unusual, especially those of the outer. Clinically, the symptoms are all referred to the joint. Genu valgum or varum may result and in some cases marked arthritis deformans. They are produced by direct force. The peculiar architecture of the upper end of the tibia, somewhat similar to that of the os calcis, favors compression fractures by indirect force. They are often comminuted.

It seems unnecessary to reproduce the x-rays. In looking at them one is struck with the marked displacement of the tibial fragment or fragments even when the fibula is not broken. Sonntag does not speak much of ultimate results, and my experience with this form of fracture has been limited. Reduction as a rule should be accomplished by marked traction, and I prefer to treat these cases with the knee flexed for the first few days, until the swelling has subsided, on a posterior angular splint, later in light plaster, which should be changed for passive motion

<sup>1</sup> Beiträge z. klin. Chir., 1906, I, p. 430.

and massage at least once a week. In fractures of the joint end when the *x*-ray shows, after reduction, any deviation from normal in the joint surfaces I should immediately correct by open incision. That is, the same principles apply here as have been repeatedly emphasized in connection with fractures in the neighborhood of joints.

We may formulate a golden rule: the nearer a fracture to a joint the more imperative an *x*-ray study and the more one should seek for anatomical perfection of reduction—a rule which does not always apply to fractures of the shaft.

**Fractures of the Leg.** Bardenheuer's<sup>1</sup> demonstration before the last German Surgical Congress, and his claims of better results after the extension treatment stimulated other clinics to investigate and compare their ultimate results. Some papers have already been published. Morian<sup>2</sup> studies all of his experience with fractures of the leg, while Bibergeil<sup>3</sup> investigates only the uncomplicated fractures of the malleoli in Körte's clinic, and Bardenheuer again presents his side through Schrecker.<sup>4</sup> No one apparently questions Bardenheuer's results. They are by no means ideal, but as far as I can ascertain his colleagues who use other treatment seem satisfied if their results are as good as Bardenheuer's. The criticism, therefore, is not of Bardenheuer's results, but of the complex method of the extension treatment and the long time that a patient must occupy a bed in the hospital. Judging from the ultimate results in the other clinics and from my own experience, Bardenheuer's methods do not show any marked improvement. In this country the element of time that a patient must occupy a bed will influence treatment, other things being equal.

I am impressed with the fact that the good results obtained by Bardenheuer are not all to be explained by extension alone. In this extension bandage the patient has, to a certain extent, free motion of the joint and passive motion and massage are not difficult. The treatment demands constant supervision. Nevertheless, it has also greater dangers than the other methods. To me this is the greatest argument against its general employment. To equal Bardenheuer's results the simpler methods must be properly carried out. For a few days the injured leg is encased in a pillow splint or some temporary bandage, and an *x*-ray is taken. The fracture is reduced, under narcosis, if necessary. If the swelling is still marked the temporary splint is reapplied. An *x*-ray is again taken. This second view allows the selection of cases for operative intervention. As I have just stated, in fractures near or into a joint it is important to have perfect anatomical coaptation which is not so essential in fractures of the shaft.

The *x*-rays having demonstrated good position of the fragments, the

<sup>1</sup> Loc. cit.

<sup>2</sup> Archiv f. klin. Chir., 1906, lxxxii, Part ii, p. 98.

<sup>3</sup> Archiv f. klin. Chir., 1907, lxxxii, p. 579.

<sup>4</sup> Deutsch. Zeitschr. f. Chir., 1907, lxxxvi, p. 547.

patient can be kept in bed two or three weeks in a temporary splint which should be changed for passive motion and massage at least once a week. In the majority of cases the plaster can be applied at the end of the second or third week. Now the patient is allowed to get up and leave the hospital to return at least once a week for dressing. In fractures near the joint I prefer massage and passive motion every few days. In fractures of the shaft there is no objection to an interval of ten days. In the so-called Pott's fracture near the ankle the foot should be over-corrected in a varus position.

This simpler treatment is undoubtedly easier than Bardenheuer's extension, and when checked with the *x*-ray and combined with frequent dressing, the results are most satisfactory.

I have kept a careful check of my own cases and fortunately have no bad results to record. When I see bad results in fractures of the leg, they are due to the fault in treatment; no *x*-ray and too prolonged fixation in plaster.

If the Germans do not adopt Bardenheuer's methods, they must at least give him the credit for reawakening unusual interest in the treatment of fractures. We need someone in America to take Bardenheuer's place. Judging from the literature only rare and isolated observations are reported. No clinics are collecting and studying the ultimate results of large groups of cases. I am inclined to think that if every hospital collected its results for the last fifteen years the surgeons in charge would begin to modify the methods of treatment. In the *Transactions of the American Surgical Association* the subject of fractures has been given but little attention, while in the German and French Congresses it has been on more than one occasion an important topic. If the general surgeon continues to neglect fractures as he did chronic non-tuberculous joint lesions the orthopedic surgeons will step in as they did in the latter, improve conditions, and receive their deserved credit.

## SURGERY OF JOINTS.

**Pathology.** In the diagnosis, and especially during the treatment, of all joint lesions one must bear in mind that motion is the function of the articulation. Unless indicated by specific circumstances of the lesion, prolonged absolute rest without motion of itself is associated with pathological changes which impair joint function. This is true also for bone. The peculiar structural development of bone is only completed and maintained by its weight-bearing function. Absolute rest of the limbs is always followed by definite, pathological, osseous changes.

The essential tissues of the joint are the synovial membrane and the articular cartilage. They are affected by etiological factors in the same manner as other tissues. The reaction differs somewhat in detail. But,

restoration, after certain changes have taken place in the synovial membrane and cartilage, is less perfect and slighter residual scar formation produces greater loss of function here than elsewhere, because of the peculiar anatomical relation of the joints to their function.

Because of these facts any destructive lesion of joints must be recognized and subjected to treatment at an earlier stage. In order to accomplish a cure with restoration of perfect function, this treatment must be instituted at that period of the disease in which complete restoration to normal is possible. Treatment instituted later may result, it is true, in the cure of the disease, but now with the joint function in various degrees of impairment up to ankylosis.

Many diseases of the joints are secondary to primary foci in the articular end of the bone, for example, tuberculosis and osteomyelitis. Others are primary in the synovial membrane or cartilage, and the bone is secondarily, or not at all, affected. Whether the origin is primary or secondary, the pathological changes in the joint are essentially the same. As regards future function, bone involvement, whether primary or secondary, makes the prognosis worse.

Except in traumatic lesions, the cartilage plays a passive part. After traumatism the cartilage only may be first affected: then a loosened piece of cartilage is the source of irritation in the movable joint and becomes the etiological factor in producing traumatic synovitis. With this exception the changes are first observed in the synovial membrane, and the articular cartilage is secondarily involved in various ways and with different results. Repair of defects in the cartilage is very slight as compared with that possible in the synovial membrane. In addition, cartilage defects, on account of interfering with perfect joint motion, may continue to be a source of constant irritation to the synovial membrane.

The joint normally contains a certain amount of serous fluid—the secretion of the synovial membrane. The latter is a sensitive and vascular tissue lined with endothelium, with a basal zone of loose connective tissue containing the vessels, resting upon a narrow zone of fat and a thick, fibrous capsule. All of these components are factors in the resultant pathological changes, whatever the irritation.

Any irritation of the joint is first associated with increase of fluid in the joint and a vascular congestion with definite enlargement of the minute bloodvessels in the synovial membrane. The character of the excessive fluid varies in different stages of the same disease and with different etiological factors.

Secondary to the congestion of the synovial membrane there is a proliferation of connective-tissue cells about the bloodvessels, and a definite new-growth of vascular synovial tissue over the surface of the articular cartilage. This new-growth shows a tendency to the formation of minute lobular projections, like the villi of the intestine, and is called villous synovitis.

The hypertrophy is not confined to the synovial cartilage border, but is present in other parts, producing folds in the synovial membrane, like the *valvulae conniventes* of the intestine.

These changes just described are most marked when the joint fluid is excessive (hydrops), when the irritation is subacute or chronic, and joint motion continues.

Due to this motion the synovial fringes are often caught between the cartilage covering the articulating bones, molded and pulled out into definite pedunculated bodies of various sizes and shapes. These may become detached and produce the so-called loose, soft-joint bodies. In very chronic lesions of long standing, fat is formed in the joint villi and pedunculated bodies and gives rise to a picture called *lipoma arborescens*.

This pannus and villus formation in the synovial membrane takes place not at all, very slightly, or to an extreme degree, in the different forms of joint lesions.

The joint fluid may be serous, serofibrinous, bloody, and purulent. A purulent effusion, with rare exceptions, is present only in association with microorganisms of a pyogenic nature. Bloody effusion characterizes certain joint lesions in hemorrhagic diseases, like purpura, hemophilia, and scurvy. It is associated with local lesions, chiefly angioma and sarcoma. It may be present after traumatism. But no quantity of blood to speak of is observed in the definitely inflammatory processes, like tuberculosis and the non-tuberculous arthritides. It is rather interesting to observe that in spite of the great vascularity of villous arthritis hemorrhage is rarely found in the joint fluid.

When fibrin is present in the joint exudate it becomes a definite factor in the pathological picture. The fibrin may collect and form loose joint bodies; more frequently it adheres to the congested synovial membrane, and later bloodvessels and new cellular tissue grow out into the fibrin organizing it. Layer upon layer of this organized fibrin may form on the surface of the synovial membrane and on the pannous growth over the articular cartilage. This is chiefly observed in tuberculous synovitis, but may be present, to a slighter degree, in any form of synovitis.

The next change in the synovial membrane is the destruction of its endothelial lining and the formation of definite granulation tissue.

Resolution to normal with restoration of joint function is possible in all forms of synovitis which have not reached the stage of granulation-tissue formation. The greater the production of granulation tissue the greater the resultant scar tissue after resolution. It is the scar tissue that impairs joint function, even though there be no cartilage defects.

The changes in the cartilage vary and are closely associated with changes in the synovial membrane and the character of the exudate. All forms of joint exudate, except the purulent, have practically no deleterious effect on the cartilage. But a purulent exudate of itself may soften, disintegrate, and loosen it.

With the formation of granulation tissue there are always cartilage defects. When the synovial membrane grows over the cartilage, especially if there is organized fibrin in this growth, the cartilage beneath suffers.

Secondary bone changes may take place through the defect in the cartilage, or beneath the synovial membrane at the cartilage border. These changes are either bone destruction or, especially beneath the periosteum, irregular bone formation.

It is not necessary to carry the description of the possible pathological changes any farther, for beyond this point the changes are simply further and greater involvement, which must result in destruction of joint function. From the standpoint of accomplishing a cure with joint function, the pathological process must be checked before it reaches this advanced stage.

Wollenberg<sup>1</sup> in a very interesting review of the pathological anatomy of chronic arthritis confirms what we have just said, except he states that he has had an opportunity to study a few joints in the very early stage. He finds that the first changes are in the cartilage and bone ends. This is a very interesting observation and should be confirmed by further investigation before accepted. The cartilage first shows defibrination and proliferation, indicating that the chemical or infectious irritant is deposited between the cartilage and bone. This is certainly true in gout.

**Etiology.** Especially during the last year numerous contributions have appeared on the etiology of non-tuberculous arthritides. The *Journal of the American Medical Association*, February 2 and 9, 1907, xlviii, contains a number of very interesting communications. In spite of the absence of definite bacteriological proof more and more investigators are inclined, from clinical and pathological studies, to the view that the majority of forms of both acute and chronic arthritis are of infectious origin. This conclusion has been of practical value in that it has led the surgeon and the physician to at once seek for a portal of entrance through which the infectious material invades the circulation and causes trouble in one or more joints. Clinical experience has demonstrated that if this area can be found and removed, the joint symptoms subside, and now local treatment of the more or less injured joint gives entirely different results. In the past treatment has been confined only to the joints, and this could not be expected to influence the area through which the joints were receiving their infectious irritant.

The tonsils stand first as the portal of entrance of non-tuberculous arthritides, except the gonorrheal. The proper and complete removal of enlarged tonsils should be considered the first step in the treatment of chronic arthritis. Dr. Gamble, of Baltimore, recently told me that he

<sup>1</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 282.

proposes to remove the tonsils at his next opportunity in the acute stage of acute polyarthritis rheumatica. In a patient with a history of a recent attack of this disease the tonsils should be removed as a prophylactic treatment against future attacks.

At a meeting of the Johns Hopkins Medical Society, Barker summarized the various portals of entrance through which infection might reach the joints, and Cole considered the relation of the gonococcus to acute and chronic arthritis. Their opinion favored the infectious origin. Baer discussed hypertrophic and atrophic arthritis, and was still of the opinion that some forms were not of infectious origin. At the same time I presented a pathological study of the experience of the surgical clinic, and was compelled to conclude that it was easier to explain the pathological changes on the basis of traumatism and infection than any other etiological factor. Baer and Rosenheim observed a very interesting case of spondylitis relieved by Rosenheim, who found a small focus of infection in the ethmoidal cells. I have observed a case of pain and stiffness in the upper cervical vertebræ completely relieved by the disinfection of a decayed tooth. It is unnecessary to multiply examples.

One, therefore, can record a distinct advance in the treatment of joint inflammations based upon the now almost universal acceptance of the infectious origin, and in the treatment there are two factors: one, the search for, and the removal of, the cause; the other, the local treatment. Hoffa,<sup>1</sup> in an interesting discussion before the Surgical Society of Berlin, favors the infectious origin of the so-called *arthritis deformans* which he proposes to call polyarthritis progressiva or arthritis destruens. I must agree with König that I see no reason for adopting, as yet, new names, and, surely, the word progressiva would make a bad mental impression upon the patient. I also agree with Barker that the general employment of arthritis deformans is unfortunate, because the patient associates it with an incurable disease, and I prefer the term acute and chronic non-tuberculous arthritis.

Among the non-infectious forms of arthritis Hoffa recognizes five: (1) Traumatic; (2) irritative (chronic hydrarthros); (3) constitutional arthritis (gout, hemophilia); (4) neuropathic; (5) functional (joint neuralgia, intermittent hydrops).

For practical purposes in the differential diagnosis and for treatment a broader classification simplifies methods. First, one must exclude a lesion of the spinal cord (tabes and syringomyelia); second, constitutional diseases like gout, hemophilia, purpura, and scurvy; now the diagnosis rests between a lesion of traumatic and one of infectious origin. The etiological factors in traumatic arthritis are to be found in the joint itself, or at some distance from the joint acting indirectly, for example, a flat-foot may produce a traumatic arthritis of the knee or hip. In infectious

<sup>1</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 280.

arthritis, with rare exceptions, a bacteriological study of the joint fluid or synovia is of value. Only in very acute arthritides can we demonstrate the gonococcus or other pyogenic bacteria, and these cases require immediate and special local treatment. In looking, therefore, for the infectious agent, tuberculin is given to seek for tuberculosis, mercury and iodide of potassium as a therapeutic test for the presence or absence of syphilis. Having excluded syphilis and tuberculosis the genito-urinary tract is searched for the gonococcus. Failing to find this, throat, nasopharynx, lungs, skin, and alimentary tract are examined as far as it is possible for a portal of entrance.

I am quite confident that, especially in early cases, the search for the etiological factor and its demonstration will result in almost brilliant therapeutic achievements. If the cause can be removed before the pathological changes, described in the beginning of this section, have extended too far in the joints, general and local treatment will cure the disease and restore function.

It requires an expert to exclude the tonsil and the nasopharynx. Large and infected tonsils may not be prominent on inspection. In men it may require frequent massage of the prostate before the gonococcus is demonstrated, and in women the endometrium infected with gonococci or other organisms may be the portal of entrance.

Many practitioners are not aware that the gonococcus may produce a polyarthritis just as chronic, progressive, and deforming as the so-called typical arthritis deformans. I have such a case under observation in which the gonococcus was found on massaging the prostate. This patient is getting well. His gonorrheal infection of the prostate has been cured, and now the joint lesions are gradually reacting to treatment.

Marsh<sup>1</sup> reports on polyarthritis due to gonorrhea, staphylococcus, streptococcus, or mixed infections with interesting examples of each. Gibney<sup>2</sup> calls attention to the rather common occurrence of *gonorrheal arthritis in children*; Zesas,<sup>3</sup> on this complication in *scarlet fever*, and Felix Franke,<sup>4</sup> in *influenza*. Taylor<sup>5</sup> and Frauenthal<sup>6</sup> discuss *syphilitic arthritis*, both hereditary and acquired.

In infectious arthritis, in certain very acute cases, practically always purulent, the gonococcus or some other pyogenic organism can be demonstrated on aspiration. In other cases, clinically, just as acute, the effusion is non-purulent, and with our present bacteriological investigations sterile. Usually such cases are called acute articular rheumatism, but this clinical picture with its pathology, serous or serofibrinous synovitis,

<sup>1</sup> British Med. Jour., December 8, 1906.

<sup>2</sup> Amer. Jour. of Surgery, November, 1906.

<sup>3</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 77.

<sup>4</sup> Deutsch. Zeitschr. f. Chir., 1906, lxxxv, p. 335.

<sup>5</sup> New York Med. Record, May 26, 1906.

<sup>6</sup> Ibid.



has been observed during or after any infectious disease, and is probably due to the toxins or organisms of attenuated virulence, either specific for the infectious disease, or secondary invaders.

The most interesting and most practical point to remember is that clinically and pathologically the degree of the symptoms and pathological changes vary with each organism.

With a gonorrheal urethritis every possible form of arthritis has been observed, and this is true of all the other demonstrable organisms. The study of gonorrhea and its joint complications has done more to clarify the subject of arthritides than anything else, because the portal of entrance and the presence of the organisms here is most accessible to demonstration.

In the general enthusiasm for the infectious origin of arthritis traumatism must not be lost sight of. As a rule the traumatic arthritis is monarticular, the infectious polyarticular. I emphasize here the importance of trauma, because at the present time our most satisfactory results belong to this group. The local defect in the joint is not always present in the x-ray, but is found at the exploratory incision. To this simple group belong loose cartilages of various kinds, joint lipoma and villous arthritis, and projecting callus of unrecognized joint fractures. These patients are immediately and permanently relieved. The cases of traumatic arthritis associated with deformities such as flatfoot, knock-knee, and coxa vara are quickly relieved by proper correction of the deformity.

**Clinical Picture and Diagnosis.** Every contribution quoted or to be quoted gives this consideration, and I think I have, in discussing the etiology, brought out some of the important facts. A recent observation can be used as an illustration. I have just seen a young man, aged twenty years, who two weeks ago was knocked down by a street car receiving a sprain of the right ankle and other contusions. There was very little swelling of the ankle, and this and the pain disappeared in twenty-four hours. He remained quiet in bed for five days on account of the other contusions. After getting up and walking for about one day he experienced pain in this ankle, felt feverish and observed swelling. When this history was given to me by his physician it at once suggested an etiological factor beyond trauma. When I saw the patient I recognized his face and then the scar on his wrist. Three years before I had opened and irrigated this wrist and the tendon sheaths for a purulent arthritis in the second week of an acute urethritis, and demonstrated the gonococcus from both places. I found that the patient had discontinued the local treatment of the urethra after leaving the hospital. This undoubtedly is a flare-up of the old trouble brought about by the trauma. Not long ago, a woman, aged fifty years, came under my observation with a history of recurrent attacks of swelling of both knees; her tonsils had been removed and she had gone through the various general and local treat-

ments, both for rheumatism and gout. In each knee-joint I found a pedunculated lipoma; since the removal of these there have been no further symptoms. Our diagnosis must, in many instances, be made by the process of exclusion, and one should rapidly, in doubtful cases, try to cover the entire field of possibilities, exclude the lesions of the spinal cord, look for the gonococcus, examine the nose and throat, try the antisyphilitic drugs, and in many cases it will be necessary to explore the joint.

**Treatment.** In previous numbers of *PROGRESSIVE MEDICINE*, I think I definitely proved that for acute arthritis in which the exudate contained the gonococcus or any other pus-producing organisms the joints should be opened and irrigated. In the last year I have ascertained the ultimate results in these cases, and this has confirmed the efficacy of the treatment which has been advocated and practised by Halsted before 1890.

In the acute arthritis in which the exudate is non-purulent and sterile, one should look for the portal of entrance. If the patient has typhoid or any infectious disease the probabilities are that the joint symptoms will subside and function will be fully restored as the general disease disappears. These joints require rest and protection, and, as the symptoms subside, passive motion and massage. When there is an effusion aspiration should be performed to exclude the presence of pus or organisms which demand operative treatment.

Riebold<sup>1</sup> advocates the intravenous injection of collargol. I have never tried it, and, it seems to me from the literature, there is a lack of confirmation of this treatment introduced by Credé.

Bier's elastic bandage for the production of *passive hyperemia* should be used in every form—acute, chronic, or subacute. For the last two years I have given it extended trials with most satisfactory results. The fifth edition of Bier's book on hyperemia and the numerous contributions to the literature place this method of treatment on a firm basis. It is unnecessary to give the voluminous references, but I would urgently advise everyone in this country to read Bier's book. The methods I have discussed in *PROGRESSIVE MEDICINE* for December, 1906.

In Hoffa's clinic it is interesting to note that in using oxygen to distend the joint, especially the knee, for the purpose of better x-ray differentiation in chronic arthritis, it was found to be a valuable therapeutic measure, even in tuberculosis. The observations are reported by Rauenbusch.<sup>2</sup> Moser<sup>3</sup> reports on his further satisfactory experience with the x-ray treatment of stiff joints, and Salfeld<sup>4</sup> claims good results from the injections of fibrolysins—an agent, I should judge, like thiosinamin.

As to the operative treatment the only advance is the demonstration by Weglowski<sup>5</sup> that cartilage can be transplanted between the resected

<sup>1</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 86.

<sup>2</sup> Ibid., p. 283.

<sup>3</sup> Mittheilungen a. d. Grenzgeb. d. Med. u. Chir., 1907, v. Mikulicz Supplem., p. 695.

<sup>4</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 193.

<sup>5</sup> Ibid., p. 481.

bone ends and a movable joint made. This promises more than transplantation of periosteum, muscle, or fascia.

In the treatment of any form of arthritis the cause—trauma, infection, or the metabolic irritants—must first be removed. Then we employ means to aid the tissues in their self-reparatory efforts which lead to restoration of joint function. The further the pathological changes have progressed the worse the prognosis for the restoration of function. As every lesion of the joint has an onset with its symptoms, the earlier we recognize them and institute treatment the better the prognosis.

**Tuberculosis of the Bones and Joints.** The contribution by König<sup>1</sup> may be looked upon as coming from the greatest authority on tuberculosis of bones and joints. It is dedicated to his colleague, Professor von Bergmann. In the introduction Professor König calls attention to the fact that this subject has been constantly one of investigation by him since the beginning of his surgical career. In this introduction he alludes to his unusually large material and calls attention to the fact that the ultimate mortality of bone and joint tuberculosis secondarily infected, which may be called suppurative tuberculosis, is about 46 per cent., while in the so-called dry tuberculosis it is but 25 per cent. This fact must be borne in mind as an argument for early and radical excision in the first group. The experience of this surgeon has been such that he feels compelled to place prominently in the introductory two pages a criticism of the point of view of modern orthopedics. The orthopedic surgeon, König claims, is prone to give first attention to apparatus with an attempt to preserve the joint function, when the nature of the local disease demands radical excision not only for the ultimate cure of the local bone-and-joint tuberculosis, but to save the patient's life. This statement impresses me as most appropriate and timely, especially now when the enthusiasm for general hygienic and open-air treatment has been incorrectly employed without local excision in this group of cases mentioned by König.

1. *General Part. General remarks on the nature, the etiological conditions, the course and the ultimate result of the disease.* König was one of the first to group together as a specific clinical and pathological entity a bone-and-joint disease which we now call tuberculosis. The discovery of the tubercle bacillus by Koch, in 1884, confirmed König's clinical and pathological studies. The older terms for tuberculosis of the joints was "extremity fungus" or "tumor albus," and for the vertebræ, ribs, sternum and bones of the skull "caries."

Tuberculosis of the bone or joint may be looked upon as primary when at autopsy only one focus can be demonstrated. Of König's sixty-seven autopsies, in fourteen (or 21 per cent.) the bone or joint focus

<sup>1</sup> Die Tuberculose der Menschlichen Gelenke, sowie der Brustwand und des Schädels. Nach eigenen Beobachtungen und wissenschaftlichen Untersuchungen August Hirschwald, Berlin, 1906.

was primary, and no other focus could be found. Such an infection can be called cryptogenic. The portal of entrance for the tubercle bacilli could not be discovered. It has either left no mark, or the focus has healed. König does not state whether the tonsils in these sixty-seven autopsies were examined microscopically. Recent investigation seems to indicate that the tubercle bacillus may enter the circulation through the tonsil. Its lodgement, therefore, in a single bone is metastatic, but for practical purposes may be looked upon as primary.

In at least 79 per cent. bone and joint tuberculosis is one of multiple foci: metastatic, of course, but must be looked upon as secondary.

König is of the opinion that in some cases trauma must be considered as the primary etiological factor, at least in localizing the tuberculous inflammation in the bone or joint. In some of these cases there is, previous to the trauma, evidence of other tuberculous foci, in others not. For an example of the first, a patient with tuberculosis of the lung develops without injury a kyphosis; after an injury to the ankle with fracture of the external malleolus, the fracture heals, but symptoms of a chronic inflammation persist with the formation of a sinus; at the operation the fracture has healed, but near it there is a focus of tuberculous caseation. As a second example, a carpenter with tuberculosis of the lung sustained a slight injury of the wrist while planing; the clinical picture of inflammation has made sufficient progress in twenty-one days to demand operation, and at the resection tuberculous osteomyelitis of the lower end of the radius with a sequestrum is found. As an example of the second, a healthy man receives a contusion of the knee; the traumatic arthritis with proper treatment does not subside, but slowly the clinical picture of a tuberculous knee develops, and at the operation there is tuberculosis of the knee-joint with a superficial sequestrum of the articular surface of the condyle of the femur. Although not mentioned by König, there is much in recent literature in regard to the relation of trauma to all forms of bone and joint diseases. Granting that the etiological factor is present in the blood, a traumatism to a bone or joint produces local conditions which furnish the organism a favorable soil not present before the injury. Such cases are frequently seen in gonorrhea and other pyogenic infections. Even in a patient suffering with syphilis a traumatism may give rise to a luetic periostitis with gumma formation.

*Heredity.* There is proof that the tubercle bacillus may pass from the mother through the placenta into the blood of the infant, and some cases of tuberculosis of bones and joints in the infant may be of this origin, although, as König says, he has never seen such an example.

*Inherited Disposition.* Before the discovery of the tubercle bacillus the majority of cases were called scrofulosis, and the minority tuberculosis. At the present time "scrofulous" may be used to describe a type of individual in whom tuberculosis of glands, skin, bones, and

joints is very common, but the term scrofulosis can no longer be employed for the pathological lesion tuberculosis. It may be retained simply to indicate that this individual or this family of children has the general appearance indicating an unusually low resistance to tuberculous infection. The exact anatomical make-up of this type is not known. Maffucci claims that in a tuberculous mother the toxins of the tubercle bacilli soluble in the blood produce definite injurious effects upon the embryo and infant, which effects lower its resistance to later tuberculous infection. Such children may be looked upon as belonging to the scrofulous type.

As to the *symptoms* of the disease, tuberculosis has not a typical course. In many cases there is nothing in the previous history to suggest an etiological factor to explain the local disease, and there may be no trauma. In some cases the opposite is true, and the diagnosis of the local lesion is made almost certain by the previous history. For example, the patient has a pleurisy with a bloody expectoration indicating lung involvement, and then the symptoms in the region of the joint. Another case suffering with tuberculosis of the kidney has a chill followed by a polyarthritis; in some of the joints there is resolution, in a few, perhaps only one, the joint symptoms persist and at the operation or autopsy tuberculosis is found.

König emphasizes that in no other disease is apparent healing more frequent than in tuberculosis of the bones and joints. The latent life or vitality of the tubercle bacillus in an encysted focus is well known. For example, a woman, aged seventy years, gives a history of tuberculosis of the ankle when ten years of age with apparent perfect healing and a free interval of sixty years; now, practically at the end of life, and after a slight trauma, all the symptoms of the joint inflammation suffered from in youth return and so rapidly that the foot must be amputated, and in the lower end of the tibia an old tuberculous focus with sequestra is found.

König does not deny that healing with scar formation is possible, but if the tuberculous process in the bone has produced a caseous sequestrum, this healing will always be apparent only, and recurrence is possible at any later interval after a slight trauma.

2. *Anatomical Remarks.* Whether the tuberculosis be primary or secondary in the synovial membrane, it is the synovial tuberculous inflammation that gives rise to the characteristic clinical picture, and whether this tuberculous synovitis be primary or secondary, the changes are the same.

The infection of the synovia produces at first synovitis with a sero-fibrinous effusion, and the characteristic changes in the tuberculous joint are dependent upon and characterized by the changes in this fibrinous deposit. The amount of fluid is of no importance. When it is excessive it produces the clinical picture called hydrops.

In brief, the fibrin is deposited in layer after layer on the articular cartilage and surface of the synovial membrane, and from the vessels of the latter the fibrin becomes organized; in this organized tissue tubercles form. The motion of the joint is an important factor in fixing the position of the first deposits and in subsequent changes.

If the knee be taken as an example, the fibrin is deposited on the cartilage from the junction of the synovia and cartilage and spreads toward the centre. This deposit on the cartilage has a gray-white color, but at the junction with the synovia, due to the new-growth of vessels, it is red—*pannus*. New layers are deposited, become organized, meet in the centre and join with the deposit from the intercondylar notch. When these deposits of fibrin are examined one finds on the surface fresh fibrin; beneath it organization of the fibrin due to vessel growth from the pannus.

This organization of the layers of fibrinous deposits in synovitis with a serofibrinous exudate is most marked in tuberculosis, but it may be present in other infections, as in the gonococcus and staphylococcus arthritis.

In the bleeder joints, hemophilia, purpura and scurvy, the fibrin comes from the bloody exudate and from the inflammatory exudate, and may produce villus formation and cartilage defects.

In tuberculosis the organized fibrinous deposits are characterized by the presence of the tubercle which at first is a lymphoid round-cell tubercle; later the epithelioid and giant cells appear.

This layer formation of fibrin with secondary vascular organization and the development of tubercles may be excessive and cover the entire joint up to 1 cm. in thickness, and the fibrinous masses may take the form of villi.

The next stage consists of secondary changes in the cartilage and bone.

At any time from the onset, when the process is simple, to the late stage when there is marked destruction of cartilage and erosion of bone, healing processes may take place with scar formation.

*Changes in the Cartilage.* These are passive, and take place either from the surface or from the bone. Destruction may take the form of small or large erosions, or separation from the underlying bone.

From the surface the cartilage beneath the organized fibrin shows various minute defects which may coalesce and form larger defects. From the depth the cartilage is separated, eroded or perforated due to a tuberculous or non-tuberculous osteitis of the bone beneath the articular cartilage.

*Bone Involvement.* The bone may be reached through surface cartilage defects or the bone may be attacked directly beneath the synovial membrane where it has no cartilage cover. Irregular osseous defects are produced.

*Changes in the Synovial Membrane.* The process is identical—layers of fibrin deposits cover the synovial membrane in all places, become organized from the synovial vessels, and the first tubercles appear in this organized fibrin, later only in the intima proper of the synovial membrane, and much later in the subsynovial fibrous tissue. This organization of the fibrin finally gives rise to a tissue resembling granulation tissue—*synovitis granulosa*.

*The Free Fibrin.* Due to the fluid and motion of the joint the free fibrin may give rise to various forms of attached and unattached bodies. If attached and multiple we have the tuberculous villous arthritis, if attached, single and large—the tuberculous fibroma; if unattached—the rice bodies and various forms of soft joint bodies.

*Caseous Suppuration. Cold Abscess.* This may take place as a caseous focus in the synovial or bone tuberculosis. The caseation is probably due to the toxins of the tubercle bacillus, and necrosis takes place in the tubercle giving rise to what is called caseous necrosis.

*The Results of the Caseous Focus.* The caseous focus may vary in size. Instead of liquefying it may calcify, become chalky, be surrounded by a fibrous wall; this fibrous tissue may grow into the caseous area, partially or completely absorb it. This may be looked upon as the healing process.

More frequently the caseous tissue liquefies and forms a cold abscess. This is not due to secondary infection, according to König, but to the toxins. The liquefied foci may become encysted with a tuberculous pyogenic membrane, or perforate into the joint, or outside the joint, produce an extra-articular abscess, which may again perforate through the skin, or by gravitation form large abscesses which appear some distance from the primary focus and secondarily perforate through the skin in a dependent position.

Now and then the cold abscess with its pyogenic membrane fills the entire synovial sac; yet there may be no focus of tuberculosis in the bone or in the synovial membrane outside this sac. Such intra-articular cold tuberculous abscesses are most frequently seen in young children between the ages of three and eight years. Motion seems to favor the production of such cold abscesses.

*The Contents of a Cold Abscess.* The liquefaction of a caseous area with degeneration of the leukocytes, epithelioid and giant cells gives rise to a liquid material which cannot be called true pus. The fluid is generally white, thin or thick, according to the amount of material, may contain calcified masses or pieces of bone, cheesy masses and fibrin; when standing, as a rule a sediment develops with a clear top. The leukocytes are few in number. In this it differs from true pus. It is important to remember that the material of a cold abscess is infectious and if inoculated into an animal will produce a tuberculosis rich in tubercle bacilli. This must be remembered in the operative treatment of the joint, because other tissues may become infected.

*Summary.* Tuberculosis of joints is characterized, first, by a synovitis with a fibrinoseous exudate. If this exudate is excessive the condition is clinically called hydrops serofibrinosus tuberculosis. In some instances the hydrops may persist. In others it is absorbed and only the fibrin remains. The characteristic feature is the deposit of fibrin on the synovia and cartilage, with its organization from the vessels of the synovial membrane.

Second, tubercles form in the organized deposit, giving rise to fibroid, granulating, fungous, nodular, and purulent forms. That is, synovitis fibrosa, granulosa, fungoides, nodosa, and purulenta. The synovial membrane proper is only later invaded by tubercles, and later still the extrasynovial tissue.

Third, along with this process in the soft parts, destruction of cartilage and invasion of bone in various degrees take place.

Fourth, at any stage healing processes due chiefly to scar formation may take place.

Fifth, suppuration or cold abscess may form from the liquefaction of a caseous focus by the toxin of the tubercle bacilli, of a focus in the bone, or the synovial membrane, or a cold abscess of the entire joint sac may be produced. These cold abscesses may perforate, infect the extra-articular tissue, form secondary abscesses of the soft parts which may perforate the skin and form sinuses, or give rise to gravitation abscesses and later sinuses. These abscesses may be single or multiple and of various sizes.

König does not describe a non-tuberculous synovitis mentioned by Krause, which is observed when the focus is in the bone. Krause claims that a reaction may take place in the neighboring joint synovia which may lead to a synovitis fibrosa with a partial or complete destruction of the joint, and yet no histological or bacteriological evidence of tuberculosis is found. Now, if the tuberculous focus perforates into the partly destroyed joint the tuberculous synovitis set up has clinically less acute symptoms, less effusion, pain, etc., while if it perforates suddenly into the normal joint there is a rapid effusion with acute symptoms and the rapid production of tuberculous synovitis.

**Tuberculosis of Bone.** König calls attention to the fact, for which we have no satisfactory explanation, that tuberculous osteomyelitis has a tendency to attack the epiphysis and then extend toward and involve the joint, while pyogenic inflammations of bone begin at the epiphysis and involve the shaft. The joint, of course is not immune to extensions from the pyogenic processes any more than the shaft to tuberculosis; but primary tuberculous foci in the shaft of long pipe bones are very rare; they are more frequently observed in the shafts of the short pipe bones.

Volkman was first to show the relation between tuberculous foci in the epiphyses and joint tuberculosis.

Bone foci of tuberculosis occur in two forms: in one, the cavity is



round or canal-shaped and is filled with tuberculous granulation tissue which may show caseation and suppuration. In the other, the cavity contains one or more pieces of bone. These sequestra as a rule are not completely detached as the sequestra in pyogenic osteomyelitis, but have vascular communication with the surrounding tuberculous granulation tissue and the spaces in this rarefied bone are filled with living tuberculous granulation tissue. The bone surrounding either focus differs: on the one hand, the bone may be sclerotic, which represents a healing process; while, on the other hand, the bone may be soft. In the latter instances infiltration of the tuberculous inflammatory process is more apt to extend. If the sequestrum is entirely separated from the surrounding tuberculous granulation tissue, one finds no tubercles or tubercle bacilli, but only caseous debris in the bone spaces. When caseation and suppuration take place in a bone focus the character of the liquid material differs in color and consistency from the pus in pyogenic osteomyelitis. In tuberculosis the pus, the granulation tissue, and the sequestrum are so different from the pus, the granulation tissue, and the sequestrum in pyogenic osteomyelitis that there is no difficulty in making the differential diagnosis.

In tuberculosis the sequestrum is usually wedge-shaped. The apex points toward the shaft, and the base toward the joint. In some instances unaffected bone of the epiphysis and cartilage of the joint separate the base of the sequestrum from the joint. In other cases the base of the sequestrum is beneath the cartilage. Now the cartilage disappears and the base of the sequestrum is seen from the joint side; its surface becomes smooth and eburnated.

For many years König had looked upon these bone sequestra as similar to infarcts due to the obstruction of a terminal artery in a bone by a tuberculous embolus, or the growth of tubercle bacilli in the artery. One of his assistants, Müller, was able to produce in goats, experimentally, bone foci by injecting tuberculous material into the vein. König accepts Lexer's work which for the first time gives the exact anatomical proof that tuberculous foci are true infarcts.

**HEALING OF BONE FOCI.** The tuberculous granulation of a sequestral focus may become encapsulated with fibrous tissue and eburnated bone, but König has never observed complete disappearance of the tuberculous tissue. For this reason recurrences are frequent, usually after trauma. That is, the bone focus may be present for years before the joint is infected. Suppuration in a bone focus and its proximity to the joint surface are the most common causes of joint infection, and when the tuberculous material enters the joint cavity it produces a tuberculous synovitis which, as stated before, does not differ from primary tuberculous synovitis.

**INFILTRATING PROGRESSIVE BONE TUBERCULOSIS, OR TRUE OSTEO-MYELITIS PURULENTA TUBERCULOSA.** Now and then the tuberculous

process is progressive. It infiltrates rapidly through the Haversian system of the compact and spongy bone, of shaft and epiphysis, and involves the marrow. This process always depends upon caseous suppuration. In some bones, like the os calcis, the process of this character is present from the onset, or it may begin from a joint tuberculosis, or a primary bone focus. Naturally, in these cases the prognosis locally and generally is bad. At first it may not destroy the bone to a large extent, but all the vascular connective tissue of the Haversian system is changed into gray tuberculous granulation tissue with caseous and suppurating foci, and in the marrow cavity large pus foci with a pyogenic membrane form. There is no rule or law as to the direction of the invasion, but border areas are not observed. There is no line of reactive demarkation.

**X-RAY DIAGNOSIS.** König again refers to this as the different joints are taken up. He looks upon the x-rays as a very important diagnostic aid. In joint tuberculosis the thickened synovia from the organized tuberculous fibrinous exudate may throw a hazy shadow, but the architecture of the bone is normal. As atrophy of bone takes place the shadow is normal, but lighter. In bone tuberculosis large caseous defects are seen, but when the sequestrum is impacted and small it does not show. If there is destruction of the articular ends, this will appear in the shadow. In early cases with small bone foci or slight joint defects a number of views should be taken.

### TUMORS OF THE EXTREMITIES.

This subject is one of especial interest, because with the proper knowledge of the different neoplasms one is in a better position to cure the disease without the mutilation of amputation. The relative frequency of the numerous possible new-growths is small, and even one with great experience only slowly acquires the ability to make the proper differential diagnosis.

In May, 1906, I read before the Academy of Medicine in Buffalo a paper on this subject entitled "The Importance of Early Recognition and Operative Treatment of Malignant Tumors; the Variation of the Extent of the Operative Removal According to the Relative Malignancy of the Tumor."<sup>1</sup>

I shall attempt in the following pages, from recent literature and accumulated experience, to give a short summary of the possible tumors of the extremities, their differential diagnosis, and their treatment.

There is no doubt that cures have been accomplished in both sarcoma and carcinoma originating in some part of the upper or lower limb, and

<sup>1</sup>The Journal of the American Medical Association, November 3, 1906, xlvii, p. 1740.

this has been done without amputation. Unfortunately, even up to the present time, amputation has been the method of choice, and I shall attempt to demonstrate that the same probability of a cure can be promised after local excision, unless the tumor has infiltrated to such an extent that its excision leaves a limb without function.

For practical purposes neoplasms may be divided into two great groups: the epithelial tumors which, in the extremities, arise from the epidermis, the glands of the skin, or embryonic misplaced islands of epithelial tissue; and connective-tissue tumors. Each group has a benign and a malignant form. In each group we recognize border-line tumors, and in the distinctly malignant variety different grades of malignancy.

As to malignancy, there are two elements: the local infiltration of the tumor, and the tendency to metastasis. This latter element must be looked upon as a sign of the greatest malignancy. In sarcoma with metastasis, so far as my own experience goes, and from the literature, a cure cannot be accomplished, even though the primary tumor and the metastatic lymphatic glands are completely removed. In carcinoma, on the other hand, cures have been accomplished by the removal of the neighboring lymphatics. In carcinoma of the breast with metastasis to the axilla, in Halsted's clinic, 30 per cent. of cases have remained well for three years after operation, and 24 per cent. have been permanently cured. The exact figures of the possible cures of carcinoma of the extremities with involvement of the glands of the axilla or groin I am unable to furnish. Unfortunately it has not been the routine practice to remove these glands in all cases, and when it has been done the extent of the axillary dissection at least has seldom been carried to that degree practised in malignant tumors of the breast. Up to the present time I have never observed an accomplished cure of carcinoma of the extremities with metastasis to the axilla or groin. There have been but a few cases, the glands have been extensively involved, and the lesion of long duration. When the glands in the axilla and groin have not been palpable it has not been the routine procedure to remove them. A certain proportion of these cases have returned with metastatic glands, but have not been cured by a secondary operation.

In a recent study of breast cancer I think I have demonstrated that, when the microscope fails to find in the axillary glands evidence of carcinoma, this cannot be looked upon as proof positive of the absence of metastasis, because in this group, in Halsted's clinic, there have been 60 cases in which a microscopic study of most or all of the axillary tissue removed failed to show any carcinoma, yet 20 per cent. of these cases succumbed to metastasis from one to nine years after operation. At the present time the majority of surgeons perform in every cancer of the breast a complete removal of the tumor, the breast, the pectoral muscle, and the axilla, whether the glands in the axilla are palpable or not. I think this rule should be applied to carcinoma of the extremities.

In attacking the local tumor, whether it be carcinoma or sarcoma, there is no question that an amputation high above the lesion most completely removes the disease, and if the facts proved that this was essential for a cure, no one would hesitate to amputate. But as I will show later, amputation is not always necessary. In attacking the carcinoma or sarcoma locally we must have a conception of its local growth. Both at first extend by local direct infiltration. In sarcoma, as a rule, the growth is more circumscribed, and the local excision need not be as extensive as in carcinoma. In the latter the infiltration very quickly extends irregularly along lymphatic channels, connective-tissue septa, and muscle fascia. Therefore, in carcinoma a wider zone of apparently uninfiltreated surrounding tissue should be removed. W. Sampson Handley (John Murray, London, 1906), in his monograph on cancer of the breast and its operative treatment, very clearly and beautifully demonstrates this fact. This work, next to Halsted's, emphasizes the importance of the complete operation for cancer, and this book has stimulated me to apply a similar research to malignant tumors of the extremities.

In the past, surgeons in this country have amputated for sarcoma and performed a rather restricted local operation for carcinoma of the extremities. From my pathological knowledge of the local growth of the two diseases, *a priori*, the reverse should have been practised. That is, amputation is indicated in carcinoma more than in sarcoma, but even in the former, in many cases, I am of the opinion that a local excision sufficiently radical can be done without removing the limb.

Both in sarcoma and carcinoma we must recognize a difference in the degree of malignancy. This will influence our local operation. In sarcoma removal of the neighboring lymphatic glands is unnecessary, because if they are involved the prognosis is hopeless. In some cases, especially of malignant pigmented mole, the glands should be removed, because, if they are not, they soon will be involved, and for the time the patient has to live he will be relieved of the mental anxiety of the palpable tumor in the axilla or groin. In all forms of carcinoma I am of the opinion that a most radical extirpation of the lymphatics in the axilla and groin should be performed, irrespective of the nature or degree of malignancy of the primary tumor, until we have estimated the possibilities of a permanent cure. One exception may be made of the basal-cell epithelioma or rodent ulcer.

**Epithelial Tumors.** In the skin the epidermis, its glands, and misplaced embryonic epithelial elements may give rise to benign and malignant epithelioma. As a matter of fact the malignant epithelial tumors without a previous history of ulcer, sinus, or some chronic inflammatory skin lesion are rarely observed in the skin of the extremities, while they are common in the lip, tongue, skin of the face, and prepuce of the penis. For this there is no satisfactory explanation. In the extremities chronic

ulcers, sinuses, old gunshot wounds, sinuses in chronic osteomyelitis, scars of burns, chronic eczema, syphilitic ulcers, x-ray dermatitis, etc., if slow in healing, are very apt, in months or years, to become the seat of a malignant epithelial tumor. That is, there must be a previous lesion of the skin of an inflammatory nature.

The malignant epithelioma of the skin appears clinically as an ulcer or a fungus, so we are constantly called upon to differentiate between the malignant and inflammatory ulcer or fungus. From my experience there should be no difficulty in making this differential diagnosis. Shortly I will give illustrative cases.

When the epithelial tumor is covered with epidermis it arises from the sweat gland, the sebaceous gland, the hair follicle, or misplaced basal or squamous epithelium. These tumors as a rule are adherent to, and covered with, normal epidermis. Now and then they are completely subcutaneous. These nodules cannot be distinguished from subcutaneous connective-tissue tumors—the fibroma, the lipoma, the neuroma, etc. The pigmented mole is recognized by its pigment and the nevus by its color. In the past the profession has looked upon these skin and subcutaneous nodules as innocent, but recent experience shows that both the epithelial and connective-tissue tumor may without warning, months or years after their onset, change their character and give rise to a malignant tumor. I have been surprised to find, in the study of sarcoma and carcinoma arising in the skin, how often there has been a history of a small, apparently innocent nodule for months or years. I am of the opinion that they should always be removed. The operation is a simple one and can be performed under cocaine anesthesia. In the last few years there have been collected in the surgical pathological laboratory of the Johns Hopkins Hospital a large number of these tumors, of every variety, and it has been very interesting to compare their histological appearance with the malignant tumors which apparently have arisen in similar nodules. This experience and the recent literature have convinced me that many patients will be spared not only more extensive operations, even to mutilation, but that their lives will be saved by the removal of these tumors while they are still small and apparently innocent.

A classification of epithelial tumors has already been given<sup>1</sup> with gross and microscopic illustrations of each type, calling attention especially to Krompecher's basal-cell epithelioma, and to Petersen's reconstruction models.

I am especially impressed with Borrmann's<sup>2</sup> study of 290 cases of *carcinoma of the skin*. His specimens were obtained from many different surgeons with the clinical history and result, and were all subjected

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1904, p. 136.

<sup>2</sup> Deutsch. Zeitschr. f. Chir., 1905, lxxvi, p. 404.

to careful microscopic study. Similar to Krompecher, Borrmann recognizes two groups: the tumor composed of the superficial epithelium, the well-known, common squamous epithelioma, and the second, arising from the deeper cells, which originally was called by many pathologists endothelioma and which Borrmann designates as corium carcinoma. It is the same group to which Krompecher has given the term epithelioma basocellulare. Borrmann questions whether there is a transitional group described by Krompecher as carcinoma cubo-cellulare, yet he speaks of a tumor as a "squamous epithelioma without hornification," which is practically equivalent to the transitional group. This histological division into squamous and corium carcinoma, or, as I prefer Krompecher's terminology, carcinoma spinocellulare, cubo-cellulare, and basocellulare, is a very important one. The tumor as a rule can be recognized clinically; if not—always histologically; for the latter, the basocellular tumor, the *x*-rays may be tried and local excision is sufficient. Personally, I prefer excision. In the last year three cases apparently cured by the *x*-ray treatment have recurred one to two and one-half years after the last treatment. For the two former groups extensive local excision with removal of the lymphatic glands is the imperative operation. Clairmont<sup>1</sup> reports on 19 cases of carcinoma basocellulare observed in v. Eiselsberg's clinic, some of which occurred on the extremities. Cönen<sup>2</sup> contributes two very extensive articles from v. Bergmann's clinic with excellent gross and microscopic illustrations. Clairmont uses Krompecher's classification. Borrmann brings out some very interesting points in the etiology of carcinoma of the skin. He is of the opinion that there is always an embryonic residue which may be just beneath the basal cells or a definite subepidermal or subcutaneous nodule (embryonal cell dystrophia). He is also of the opinion that there must be some exciting cause which stimulates these cells to take on activity resulting in a neoplasm.

Rarely it is a single trauma, but it is quite possible that a single trauma may give rise to the new-growth. As a rule it is recurrent trauma, or some form of chronic irritation; for example, the carcinoma of the scrotum in chimney-sweeps; carcinoma of the lips in pipe smokers. As Borrmann remarks, it is quite true that many individuals who do not use the pipe suffer from carcinoma of the lip; and many who do, do not get carcinoma of the lip. Everyone who suffers from a carcinoma of the lip must have, in the first instance, an embryonic residue. In many instances the evidence of an embryonic residue is demonstrable by the presence of a small epithelial wart or corn, an epidermal or subcutaneous nodule which has been quiescent for years and which, after a single trauma, perhaps, or some form of irritation, grows, ulcerates, and gives rise to an ulcer or a fungus.

<sup>1</sup> Zentralbl. f. Chir., 1907, xxxiv, Supplem. No. 31, p. 3.

<sup>2</sup> Archiv f. klin. Chir., 1905, lxxvi, p. 1100; and 1906, lxxviii, p. 801.

In the extremities these little warts and subcutaneous nodules should be regarded with suspicion, and the possibility of a malignant epithelial tumor in a chronic ulcer or sinus, or any chronic inflammation, borne in mind. I have seen, and the literature records carcinoma in the sinus of an old bullet wound, in sinuses of chronic osteomyelitis, in old leg ulcers, in the scar of an old burn, in psoriasis, in senile keratosis, in lupus, in blastomycetic dermatitis, etc. I have an example of more than one of each in the surgical pathological laboratory. Borrmann, among his 296 cases, collected only 7 from the extremities. So his experience is comparatively small.

Carcinoma of the skin has been the title of many interesting monographs, beginning in 1890, by Volkmann, who collected 223 cases from the literature and reported 39 observations from his own clinic during twenty years. The most recent is by von Brunn,<sup>1</sup> who collected 368 cases from the literature; 20 from his own clinic in the last twenty years. The etiological points discussed by Borrmann are confirmatory of the statistical studies of these larger groups of cases. Von Brunn takes the stand which I have already advocated, that the lymphatic glands should always be extirpated if they are palpable, although their enlargement may be inflammatory. I would go further and advise their excision whether palpable or not.

In performing a local excision for carcinoma of the extremity the tumor should be removed with a wide zone of apparently healthy skin, a wider zone of subcutaneous fat, fascia of muscle, and muscle. Borrmann has shown by the microscopic study of the edges of the tissue removed how not infrequently it has not been given sufficient berth by the operator.

Fig. 9 is a beautiful example of a malignant epithelioma spinocellulare in blastomycetic dermatitis, which I have recently excised, and Fig. 10 represents a healed area of the inflammatory disease on the forearm. The skin lesion had been present a number of years; the tumor formation three months. Fig. 11 demonstrates that we may have a benign epithelial growth in the scar of a burn. This patient was forty-eight years of age, the original burn thirty-one years previous to admission, the present growth of seven years' duration. Histologically it was a benign epithelioma spinocellulare. Local extirpation was sufficient. Wikhoff<sup>2</sup> has found calcified areas and bones in such tumors. In his case the tumor followed the bite by a dog and had been present ten years in the calf of the leg. Fig. 12 is an example of a malignant squamous epithelioma in the scar of a burn; the diagnosis could be made from the surface of the ulcer. The patient was thirty-two years of age, the scar of seventeen years' duration, the ulcer of three months' duration. In this case the zone of skin removed is too narrow, and in Fig. 13,

<sup>1</sup> Beiträge, 1903, xxxvii, p. 227.

<sup>2</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 550.

a photograph of the section through the ulcer, infiltration of the new-growth can be seen. This was proved by microscopic section, reported and local recurrence prognosticated. A second operation was performed



FIG. 9

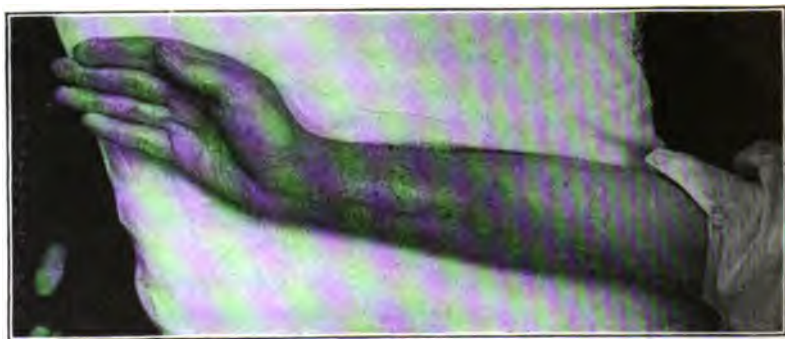


FIG. 10

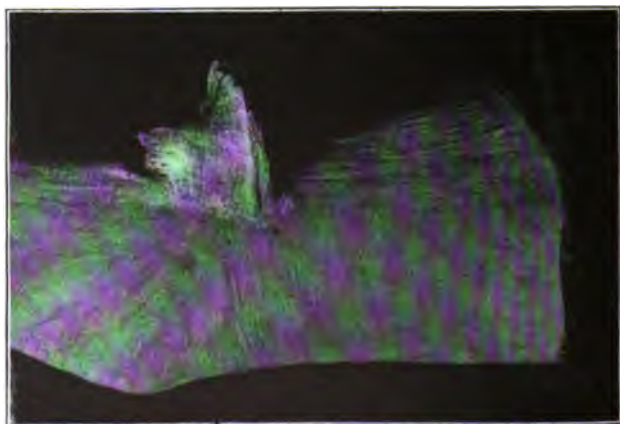


FIG. 11



and remains of the carcinoma demonstrated. In this variety of tumor not only must the local excision be wide, but also deep, and the neighboring lymphatics excised. Fig. 14 is an example of a carcinomatous ulcer in

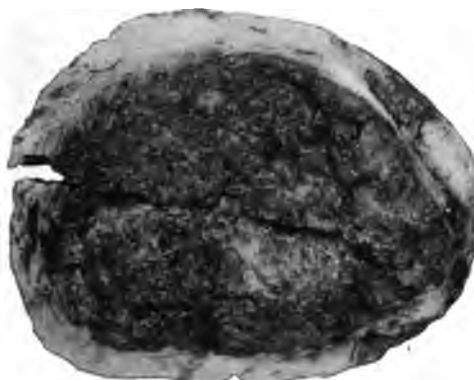


FIG. 12



FIG. 13



FIG. 14

an old gunshot wound in the ankle which had been received thirty years before; the recurrent ulceration was of three years' duration. At the first operation an attempt was made to remove the disease by excision; at the pathological examination incomplete excision was demonstrated and the glands of the groin were completely excised; they did not show microscopic metastasis. This patient was well seven years since operation. Fig. 15 illustrates an example of a carcinoma arising in a subcutaneous nodule which had been present twenty years. The ulceration and fungous growth were of eight months' duration. It is a typical mushroom fungus and histologically a carcinoma cubocellulare, a very malignant epithelial tumor. Figs. 16 and 17 represent the surface and sectional views of a carcinoma which arose after repeated trauma in a subcutane-



FIG. 15

ous nodule of many years' duration. In this case undoubtedly the original tumor had been a congenitally misplaced area of sweat-gland epithelium. Fig. 18 is a beautiful picture of the clinical appearance of a fungous epithelioma basocellulare solidum malignum. This patient, aged forty years, has numerous congenital tumors; in the one shown in the illustration there has been growth, ulceration, and fungus formation of eight months.

I trust these cases, when added to those previously illustrated in PROGRESSIVE MEDICINE, will graphically emphasize the important clinical and pathological facts which must be understood in the treatment of epithelial tumors of the extremities.

**Connective-tissue Tumors.** As compared with the epithelial, the benign and malignant tumors of connective tissue arising in the extremities



FIG. 16

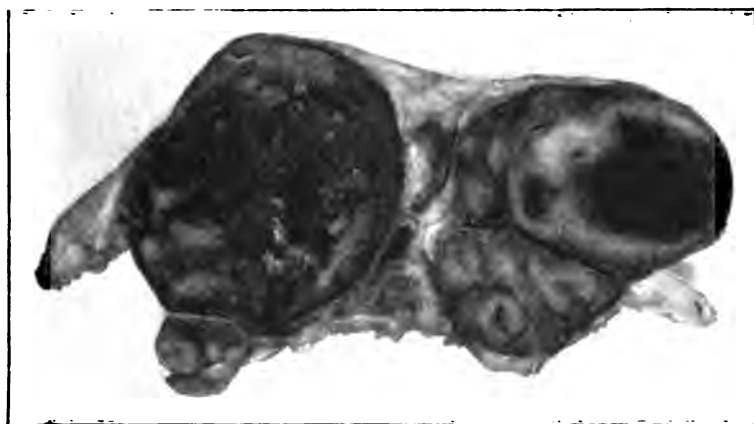


FIG. 17



FIG. 18

are much more common. They appear as subepidermal, subcutaneous, and deeper nodules. In the differential diagnosis we must distinguish between the benign and malignant tumor and inflammatory masses, for example, gumma, tuberculosis, the different forms of myositis, etc.

With the exception of the lipoma and the osteoma, every benign connective-tissue tumor may become malignant. This fact must be borne in mind in our attitude toward innocent nodules of congenital origin, or present a number of years.

The study of the benign connective-tissue tumors forces one more and more to the conception of the origin of neoplasms from congenital residues of cells.

There is no doubt that many sarcomas arise in these benign connective-tissue tumors. In such sarcomas the relative degree of malignancy is less, and the more one finds evidence of the benign tumor the better the prognosis. The etiological factor that excites the sarcomatous activity in the benign neoplastic tissue is very difficult to demonstrate. Many pathologists and surgeons from clinical studies look upon trauma or any inflammatory irritation as a definite factor. For this reason, innocent nodules, even though quite small and giving no discomfort, should be removed if there is a history of a recent trauma or if their position is one in which recurrent slight trauma is possible.

As to sarcoma, which arises without a history of a previous benign neoplasm and in which, histologically, there is no evidence of this benign tissue, there is great difference of opinion. Traumatism and any form of irritation apparently play a part.

I wish to emphasize the practical importance of this view on the relation of trauma to sarcoma. Undoubtedly, thousands of people receive traumatism and sarcoma never develops in the injured tissue. Clinically, a contusion is associated with laceration of tissue and there is always more or less blood and lymph exudate. Granulation tissue must be thrown out to fill the defect. The life history of such granulation tissue is short, and the histological result is scar tissue which in time becomes more and more absorbed. One, therefore, should expect, after a contusion, immediate swelling. This is greatest at first, due to the fluid leaking into the soft parts of the lacerated cavities. The swelling, then, at first is soft. As it is replaced by granulation tissue it becomes smaller, but still remains soft. As the granulation tissue changes into scar tissue the tumefaction becomes less and less, and firmer in consistency, and finally disappears. Therefore, after a contusion we should expect immediate swelling to be followed by a gradual but distinct disappearance. When the swelling remains stationary and then gradually increases, one should suspect a neoplasm. This clinical history is so frequent in sarcoma of the soft parts and bones of the extremities that it should make clinicians more alert to its significance. Weeks and

months are often lost, because the swelling is looked upon as an inflammatory mass after traumatism.

When after a contusion there is no immediate swelling or only a very slight one, and then, after an interval the appearance of a definite tumor, this clinical picture should be considered sufficiently significant of the possibility of sarcoma to justify exploration.

These clinical facts I have dwelt on before in the pages of *PROGRESSIVE MEDICINE*. Practically, every contribution to the subject of tumors mentions it in the discussion. In spite of this these tumors come to operation at too long a period after the first symptom. In my personal experience the period of time in which the patient delays before he seeks the advice of a physician is on the whole shorter than the procrastination of the physician.

The prognosis in a large group of sarcoma, when subjected to early operative removal, is unusually good. Metastasis is late. In the more malignant varieties metastasis takes place very early. Nevertheless, fortunately, isolated examples of permanent cures are recorded at intervals in the voluminous literature. In these cases the tumors were small and operated upon very quickly, weeks rather than months after the first symptom.

In the following discussion I shall, so far as possible, bring together the benign and the resultant malignant tumor.

**CONGENITAL PIGMENTED MOLES.** There is much difference of opinion in regard to the embryonic origin of these subepidermal masses of pigment-forming cells. Unna, Krompecher, and others are of the opinion that they are epithelial cells of the basal type misplaced early in embryonic life, and for this reason look upon the tumors as epithelioma. Clinically and histologically, both the benign pigmented congenital mole and the pigmented alveolar sarcoma which arises in them differ from the basal-cell or corium epithelioma. The congenital tumor is more pigmented, the morphology and arrangement of the cells have distinct differences. The congenital mole usually is visible from the first; the basal-cell epithelioma is seldom distinct until later in life, usually after forty. When the congenital mole becomes malignant, usually after fifty, the local growth in the primary tumor is small, it metastasizes early through blood and lymphatics, and there are no recorded cases of a permanent cure. When the basal-cell epithelioma becomes malignant the local growth is slow, progressive, and if not removed it gives rise to a large superficial fungus or an ulcer of wide extent (the rodent ulcer). Metastasis is unique, and in my experience, when this has taken place, histological examination of the primary tumor demonstrates a mixed variety.

For this reason the congenital pigmented mole and its sarcomatous degeneration belong to a class of tumors by themselves, and more closely resemble the sarcoma than the carcinoma.

In *PROGRESSIVE MEDICINE* for December, 1903 (p. 149), and later in 1905 (p. 260), the importance of removing all large congenital pigmented moles was carefully discussed. As a rule the duration of life between the onset of growth in the innocent mole and death from metastasis is less than one year. Now and then there are exceptions to this rule. In a patient whom I saw through the courtesy of Dr. Crile, of Cleveland, there was a pigmented mole beneath the nail of the toe and a mass of glands in the groin. The patient stated that these glands had been present at least three years. At the operation Dr. Crile explored the abdomen, and found no evidence of metastasis; he then made the inguinal dissection and amputated the toe. The primary and metastatic tumors were pigmented, alveolar sarcoma. In a case which I<sup>1</sup> have previously illustrated the patient lived eighteen months after the amputation of the thumb for a malignant, pigmented, alveolar sarcoma which had been present at least eighteen months. Olbert<sup>2</sup> reports a case in which twenty-four years after enucleation of the eye for a pigmented



FIG. 19

alveolar sarcoma of the chorion the patient died of multiple pigmented, alveolar, sarcomatous metastases without local recurrence. In such an observation one is always suspicious that there was some mistake in the diagnosis of the primary tumor and that the metastases really took place from another tumor of more recent origin and overlooked. Figs. 19 (*a* and *b*) are photographs of the surface and sectional view of a benign pigmented mole which in my experience later in life would be very apt to become malignant.

I have recently had under observation a patient aged fifty-five years; seventeen months ago he had removed from the right forearm, by electricity, a small pigmented mole which had recently shown growth; there were five treatments during a period of ten days; one month after the operation he noticed a small gland in the axilla which had been gradually increasing in size. At the operation I found the entire axillary glands involved, yet the patient was in good health and there was no evidence of internal metastasis. However, this is frequently so.

<sup>1</sup> *PROGRESSIVE MEDICINE*, December, 1905, Fig. 31, p. 261.

<sup>2</sup> *Zentralbl. f. Chir.*, 1906, xxxiii, p. 599.

In my experience and from the literature, I have been unable to find a definite cure. A colleague showed me the section of a mole from the face and the gland in the axilla. This patient remained well four years after operation. However, the histological appearance of the mole was benign, and there was no evidence of metastasis to the glands. It is only such cases incorrectly interpreted that get into the literature as cures.

**CONGENITAL NEVI AND ANGIOMA.** The congenital tumor in the skin is recognized by its color which disappears under pressure; the deeper tumor by its compressibility and change in size. Apparently sarcoma in a congenital cutaneous nevus is much less frequent than in a pigmented mole.<sup>1</sup> When a congenital nevus becomes malignant the thin epidermis over the growing tumor ulcerates and a fungus follows. Metastasis takes place later than in the alveolar sarcoma, but the tumor is very malignant, and permanent cures are not often recorded. How often the subcutaneous angiosarcoma arises in a benign angioma is difficult to estimate.

The most common situation of the deeper tumor in the soft parts is intramuscular.<sup>2</sup> As intramuscular angiosarcoma is very common, I am impressed that there may be an etiological relation between the benign and the malignant tumor. Dr. Stage Davis, of Baltimore, has just collected over 100 cases from the literature and finds very little reference to sarcomatous degeneration. Recurrences are not infrequent after partial operations, but the recurrent tumor is still histologically and clinically benign. There is, therefore, no justification for an extremely radical operation for primary angioma of striated muscle. Küttner,<sup>3</sup> Pagenstecher,<sup>4</sup> and Reclus and Maystot<sup>5</sup> are the most recent contributors to this voluminous literature. Küttner, in his cases, discusses the presence of fat and bone in the cavernous angioma of muscle.

The benign angioma is easily recognized by its red, spongy, compressible tissue and the blood which is expressed on pressure.

In this group of tumors it is very important to know that there may be an angioma, a perivascular growth of cellular fibrous tissue which gives rise to a tumor that might be mistaken clinically and, at first sight, histologically, for a sarcoma. These are called fibro-angioma or elephantoid angioma.<sup>6</sup> Fig. 20 is the photograph of a gross section and shows the brown, red, spongy areas of angioma, and the white areas of cellular fibroma. It was a pedunculated tumor on the skin in a girl aged

<sup>1</sup> *PROGRESSIVE MEDICINE*, December, 1903, pp. 149 and 152.

<sup>2</sup> *Ibid.*, December, 1905, p. 242.

<sup>3</sup> *Beiträge z. klin. Chir.*, 1906, li, p. 80.

<sup>4</sup> *Zentralbl. f. Chir.*, 1907, xxxiv, p. 519.

<sup>5</sup> *Revue de Chir.*, 1907, xxvi, No. 5.

<sup>6</sup> *PROGRESSIVE MEDICINE*, December, 1903, p. 154; *International Clinics*, April, 1904, i, Fourteenth Series, p. 240.

sixteen years, and had been present five years; the skin over the tumor was cyanotic and the veins dilated.

There are two varieties of angiosarcoma: one due to the proliferation of the perithelial cell—the perithelial angiosarcoma, and the other to that of the endothelial cell—the endothelioma. In my experience, the sarcoma arising from bloodvessels is usually of the perithelial variety, while that arising from the lymphvessels an endothelioma. The latter, as a rule, has a more distinctly alveolar arrangement in the fresh and a marking somewhat like a cross-section of striated muscle or an exophthalmic goitre. It is pearly white in color and, as a rule, with the knife one can scrape a milk-like secretion. These endotheliomas are relatively very malignant.<sup>1</sup>



FIG. 20

The perithelial angiosarcoma is usually specked with red; in other places it has the same white color as the endothelioma, but is less distinctly alveolar. The patient was a child six months of age, and the tumor of the forearm shown in Fig. 21 had been present four months. An exploratory incision had been made into the tumor four days before I saw the patient; it was situated between the extensor muscles and could be completely removed by local excision. In my experience both lymphosarcoma and hemangiosarcoma rank next to the pigmented alveolar sarcoma in malignancy.

Von Hansemann<sup>2</sup> calls attention to the relation between certain sarcomas and angioma. His tumors were present shortly after birth, usually on the fingers and toes, and he found, after removal, examples of recurrence from a few to thirty years later; the recurrent tumor some-

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1903, p. 166, Fig. 32.

<sup>2</sup> Zeitschr. f. Krebsforschung, iii, No. 2; reviewed in Zentralbl. f. Chir., 1905, xxxii, p. 1030



times resembled the primary, more frequently it was more cellular and in some cases has given metastases. These tumors may arise from blood or lymphvessels, may be endothelial or perithelial in architecture. He calls them sarcoma angioplasicum.

**FIBROMA.** There is no tumor more difficult to interpret than the manifold varieties of this so-called simple connective-tissue tumor. It occurs in the benign and malignant form in all tissues. The tumor clinically benign may histologically be so cellular that it is practically impossible, in some cases, to distinguish it from a sarcoma. These are the border-line tumors; some may contain giant cells. Trauma is an



FIG. 21

important etiological factor. They are common on the gums, in the tendon sheaths of fingers and toes, and in the skin; they are seen along tendon sheaths and in the skin in diseases like rheumatism (fibroid nodules). If removed by enucleation or partially, they recur. The benign tumor is not always distinctly encapsulated.

When we study these cases histologically and demonstrate the formation of fibroblasts and fibrous tissue from the cellular portions of the tumor, this is an indication of its innocence. The greater the number of round cells, the fewer the fibroblasts, and less the fibrous tissue, the greater the malignancy of the tumor.

The cicatricial *keloid* is a tumor of unusual interest. It is a diffuse

growth in scar tissue, very cellular, and recurs after excision. Yet, if let alone it seldom reaches great size and may spontaneously disappear. Although, histologically, in its early stage it is as cellular as a spindle-celled sarcoma, yet, in my experience and from the literature, I have been unable to find any examples of a sarcoma arising in a cicatricial keloid, while, a priori, one would expect it to be very common. In the sarcomas which arise in scar tissue there is no definite previous keloid growth.

These keloids often contain elastic tissue.<sup>1</sup>

I have previously discussed fibroma of the skin and sarcoma.<sup>2</sup> Fig. 22 is a photograph of a fresh section of a subcutaneous fibrospindle-celled tumor of three months' duration in a colored girl, aged twenty years. Whether this should be called a sarcoma or a fibroma is an open question.



FIG. 22

Practically the fibroma and fibrospindle-celled sarcoma do not recur if completely removed. The largest number of cured cases of sarcoma belong to this group. Cures have been accomplished even though the tumor was composed chiefly of round cells and has produced a large fungous growth.<sup>3</sup> Durlacher,<sup>4</sup> in discussing subcutaneous, solid tumors of the fingers, brings out the point of the difficult differential diagnosis histologically between the benign and malignant tumor.

**GANGLION OF THE FINGERS AND WRIST.** It seems appropriate here, in connection with the fibroma and fibrospindle-celled sarcoma, to mention the ganglion, as it frequently occurs in the same location and cannot always be differentiated clinically. The solid tumor should be removed.

<sup>1</sup> Taddei, *Zentralbl. f. Chir.*, 1906, xxxiii, p. 189.

<sup>2</sup> *PROGRESSIVE MEDICINE*, December, 1903, pp. 158, 170 and 173

<sup>3</sup> *Ibid.*, December, 1903, p. 177, Fig. 37.

<sup>4</sup> *Zentralbl. f. Chir.*, 1907, xxxiv, p. 57.

Küttner,<sup>1</sup> from a study of 170 cases of ganglia, is of the opinion that operation is not indicated; 79 per cent. of ganglia appear on the dorsal surface of the wrist or fingers. They are very rare on the volar surface. He has also found them near the knee and ankle-joint. The ganglion may be bilateral—in about 3 per cent. of cases—and these have always been situated on the wrist. Carpal ganglia, which are the most common, are observed chiefly in young females between the ages of ten and twenty-five years; those on the knee and ankle in patients over thirty. As a rule, there is a history of a single or repeated trauma. If left alone they show a tendency to disappear. If operated upon in the active state recurrence is the rule, even with extirpation. A ganglion, therefore, should be left alone, unless size and discomfort demand its removal. The patient should always be told of the possibility of the recurrence. It is my opinion that ganglia should, at least, be explored, first, because a solid tumor demanding removal must be excluded; second, there is at least 50 per cent. chances of a cure from complete or partial removal of the sac, and if there is a recurrence, it is no worse than the primary tumor. In ganglion, however, one should never sacrifice important tissue in order to make a radical excision, while in the solid tumors everything should be removed.

It is important to remember that all cystic tumors in the region of the hand are not ganglia. Klein<sup>2</sup> records 4 cases of epithelial cysts. They were of cherry size with a distinct capsule and the characteristic granular contents of a dermoid; they were lined by squamous epithelium with hornification. Trauma was an etiological factor. Such cysts should be completely removed.

The different possible finger tumors which are of great interest and practical importance to the surgeon from the standpoint of accomplishing a cure without mutilation, I have previously considered.<sup>3</sup>

**SARCOMA IN SCAR TISSUE.** Recent literature collects much evidence in favor of the irritative origin of tumors as against the parasitic. Herberg<sup>4</sup> records a sarcoma arising in an area in which there was scar tissue from retained particles of coal. The patient was forty years of age; at the age of six years, thirty-four years ago, the skin had been wounded by a piece of coal and some of the particles had remained and were visible as a blue spot on the forehead. This area remained quiescent until six months before operation. It then grew into a small, diffuse area which was looked upon as a fibroma. Histologically, in addition to the pigment and giant cells the tumor was so cellular that it was diagnosed a sarcoma. Herberg advises the removal of all such foreign bodies, because of the possibility of future trouble. This case was of great

<sup>1</sup> *Zentralbl. f. Chir.*, 1905, xxxii, p. 1333.

<sup>2</sup> *Ibid.*, 1907, xxxiv, p. 56.

<sup>3</sup> *PROGRESSIVE MEDICINE*, December, 1905, p. 262.

<sup>4</sup> *Deutsch. Zeitschr. f. Chir.*, 1906, lxxxi, p. 506.

interest to me, because I<sup>1</sup> have observed a tumor of similar etiology. In my case the interval between the trauma with coal-dust deposit and the tumor was four years. In spite of radical local excision the patient died of internal metastasis one year after operation. Herberg's case was well eighteen months after operation. In the last two years I have removed two areas pigmented with coal-dust. Histologically, there was no evidence of sarcoma. The number of cases of this character is small, but when a tumor is observed in such an area it should be promptly and completely removed. In my case just mentioned there had been a previous incomplete operation, so it is quite possible that this patient's life might have been saved by a more radical, primary extirpation.



FIG. 23

**ELEPHANTIASIS.** This rare and interesting condition, chiefly observed in its exaggerated form in the lower limb, is not difficult to diagnosticate, as shown in Fig. 23, a photograph presented to me by Dr. C. B. Ingraham. In the surgical clinic of Professor Halsted there has been observed during the eighteen years but one example of this disease. I mention it here to call attention to the good results following the excision of huge wedge-shaped pieces of tissue from groin to ankle which has been practised in the Breslau clinic of v. Mikulicz. It is more common there, as they

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1903, p. 157, Figs. 18 and 19.

have seen from one to two cases a year. These cases are reported with illustrations by Schmidt.<sup>1</sup>

In this country we see more frequently moderate degrees of elephantiasis of the lower limb, scrotum, and penis following the complete extirpation of the lymphatic glands and vessels in the groin. It is these observations that contra-indicate the operation, except for malignant tumors and tuberculosis which resists hygienic treatment. In the past it had been the custom to perform radical operations for gonorrheal and other pyogenic infections. This is rarely, if ever, indicated. Riedel<sup>2</sup> reports on his unfortunate experiences with this complication. In the few cases which I have observed the patients have slowly, but fully, recovered. The treatment has been bandaging, bathing, and keeping the skin, especially over the scrotum, dry with powder. There is always a weeping of lymph. I<sup>3</sup> have also called attention to the possibility of elephantiasis in stumps after amputation, if the wound has been infected and followed by a chronic obliterating lymphangitis, and to the not infrequent occurrence of papillary epithelial hypertrophy in the skin associated with elephantiasis.

This complication in the upper extremity after complete removal of the axillary glands and lymphatics is less frequently observed and is never severe in degree. Experience with the ultimate results of the complete operation for carcinoma of the breast has been most favorable in regard to the arm. True, there is some edema which may be present off and on for a number of years, and when the patients are informed of this possibility, I find that it gives them no trouble or anxiety. Even when the glands above the clavicle were removed at this operation we have observed no troublesome complications on the part of the arm. In both groups of cases if the involvement of the axilla and neck is hopeless, extreme swelling of the arm may follow operation. In these cases the lymphatics are undoubtedly blocked by carcinoma, which interferes with collateral circulation.

**FIBROMA MOLLUSCUM.** This tumor is of less interest to surgeons because it is a multiple lesion. Now and then, however, it may occur over such a small area that the entire disease may be removed. Such an example is shown in Fig. 24. This patient was a male, aged twenty years, and the tumor shown in the photograph had been present since birth. They followed the distribution of the peripheral nerves.

Tumors arising from nerve sheaths are not uncommon. The single tumors are frequently pure myxomas,<sup>4</sup> and I have recently observed a similar case in the popliteal space which looked at first like a colloid goitre. These single fibromas of nerve sheaths should be radically

<sup>1</sup> Beiträge z. klin. Chir., 1904, xlv, p. 595.

<sup>2</sup> Archiv f. klin. Chir., 1906, lxxxi, p. 202.

<sup>3</sup> PROGRESSIVE MEDICINE, December, 1904, p. 144, Fig. 11.

<sup>4</sup> Ibid., 1905, p. 271.

removed locally. They may be multiple in the nerves. I have reported such an example.<sup>1</sup> After the removal of the tumor in the popliteal space by resection the patient returned in a year with multiple tumors in the sciatic nerve in the thigh, and the leg was amputated. The patient remained free from recurrence about two years, and is now dying with a tumor in the stump and multiple nodules in the pelvis. This possibility, therefore, should be borne in mind in the prognosis. First, the single tumor may be a sarcoma rather than a benign fibromyxoma; second, the multiplicity of the tumors may not manifest itself until later. They may be confined to a single nerve, and in some instances are present on the nerve roots near the spinal vertebræ. Rimann,<sup>2</sup> in reporting a multiple tumor following the branches of the sciatic in the limb, states that Garré found that in 12 per cent. of v. Recklinghausen's disease sarcoma develops later. Kren,<sup>3</sup> in reporting



FIG. 24

his case, mentions the frequency with which neurofibromatosis is associated with other congenital tumors like moles and nevi and with various congenital defects, especially idiocy. He states that as yet the experience with the x-ray treatment of this disease has shown no definite results.

**GANGLIONEUROMA.** Glinski<sup>4</sup> reports one of these rare cases. It was situated in the neck and contained ganglion cells and nerve fibers; it apparently arose from the sympathetic. I<sup>5</sup> have previously mentioned a ganglioneuroma (Custodis' case) of the peroneus nerve. I have been unable to find an example of a malignant tumor originating in these ganglioneuromas. For this reason, I think one should hesitate before

<sup>1</sup> PROGRESSIVE MEDICINE, December, p. 272.

<sup>2</sup> Beiträge z. klin. Chir., 1907, liii, p. 800.

<sup>3</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 323.

<sup>4</sup> PROGRESSIVE MEDICINE, December, 1905, p. 248.

<sup>5</sup> Ibid., p. 23.

resecting such a tumor if it occupies a motor nerve, unless suture could afterward be performed with great probability of a good result.

**LIPOMA.** Joint and osteoperiosteal lipomas, which are very difficult to diagnose before they are explored, have been mentioned.<sup>1</sup> Dege<sup>2</sup> reports on some interesting cases of intermuscular lipomata of the extremities. His observation was situated in the biceps muscle and could be palpated only when the muscle was relaxed. He collects 23 cases from the literature, about equally distributed between the upper and lower limbs. This experience shows that the deeply seated intermuscular lipomas may not be recognized from a hemangioma, a gumma, a tuberculous myositis, or a sarcoma, until exposed at the exploratory incision. The wide distribution of lipoma is commented upon, and like the dermoid cyst must always be placed among the possibilities in the differential diagnosis of a tumor formation. Next to the subcutaneous lipoma the intermuscular is most frequent. During the past year I have removed a lipoma situated between the major and minor pectoral muscles which suggested a sarcoma; one in the popliteal space that I thought at first was a fibromyxoma of a nerve sheath; one in the knee-joint which gave all the clinical signs of a chronic joint hydrops, and one springing from a defect in the lumbar vertebræ, present since birth, that could not be differentiated from spina bifida.

**MYOMA.** Tumors of striated muscle are much less frequent than of the smooth muscles, and multiple myomas of the skin of the extremities, according to Bogoljubow,<sup>3</sup> are one of the rare dermatoses. There are but 20 cases in the literature, the last report in 1901. In his case they were present both on the extremities and body; there was slight impairment of the sense of temperature in the epidermis over the tumor, and the patient experienced pain when there was a definite change in the external temperature. Bogoljubow is of the opinion that these tumors have a similar relation to peripheral nerves as the neurofibromas. During the year I had an opportunity to see a young woman, aged thirty-five years, with multiple shot-like tumors occupying chiefly both arms and the lower limbs. From the distribution and character of the tumors I looked upon the lesion as multiple fibroneuromata. I excised six tumors from various places, and each proved to be a cyst with contents like that of a dermoid or atheromatous cyst and microscopically lined by epithelium.

**Bone Tumors.** At the meeting of the American Orthopedic Association in Washington, on May 8, 1907, three papers were read on the subject of *sarcoma of bone*. Roswell Park, of Buffalo, confined himself chiefly to a discussion of the etiological factor in malignant tumors, and again emphasized his well-known conclusion that they are of parasitic origin.

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906, p. 224.

<sup>2</sup> Zentralbl. f. Chir., 1907, xxxiv, p. 311.

<sup>3</sup> Ibid., p. 550.

Coley, of New York, presented his large and very interesting experience not only with the operative results, but with his treatment with toxins. These results have been published.<sup>1</sup> In this paper Coley considers fully and very interestingly the diagnosis, treatment, and prognosis of sarcoma of the long bones, and reports 69 cases. There is a number of excellent illustrations. I cannot agree with him that the toxins had anything to do with his recorded cures of giant-celled sarcoma, because my own experience and the evidence in the literature clearly prove that equally good results have been accomplished by operative treatment without the toxins. Coley's results in apparently inoperable cases and in the more malignant forms of sarcoma of bone seem to show that the toxins have had some curative effect, but they are isolated cases and exceptions to the general rule. In a careful study of the literature extending over many years I have found similar isolated cases of the more malignant forms of sarcoma of bone which have remained well after operation sufficiently long to be considered cured.

With the addition of toxin Coley favors local excision in preference to amputation. It is my opinion that amputation for sarcoma of the long pipe bones is only indicated when the local growth has progressed to such an extent that its complete removal would result in a limb without function. As a matter of fact, the recorded cures among the more malignant tumors have been more frequent after excision than after amputation, although the number of cases subjected to amputation has been far in excess. This does not mean, of course, that the amputation would not have produced a cure, but that the tumor was so small that the operator felt justified in performing resection, and it is also of interest to note that in some of these cases resection only was performed, because the patient refused amputation.

The most impressive thing in Coley's paper is that he has accomplished cures in 8 cases of round-celled sarcoma and in 2 of spindle-celled sarcoma, in which, with the use of the toxin and local excision, the limb has also been preserved.

Unfortunately the terminology used to designate sarcoma of bone does not always give a positive idea of its correct histology. In a report from one of the largest clinics in this country, in which the patient died from metastasis of the lung after amputation at the shoulder-joint, the tumor was called a pure giant-celled sarcoma. Yet, the description and the illustrations showed a very cellular, mixed, round-celled and spindle-celled sarcoma with a few giant cells. Such a tumor is not a giant-celled sarcoma. Quite frequently the term spindle-celled sarcoma is applied without discrimination to the comparatively benign fibrospindle-celled tumor and to the extremely malignant cellular tumor in which there are no fibroblasts, nor fibrous tissue.

<sup>1</sup> *Annals of Surgery*, March, 1907.



It is very important, in order to estimate the curative value of the toxins, to have not only a very careful description of the cellular pathology of the tumor, but its location, its size, whether medullary or periosteal, whether circumscribed or diffuse, and its duration.

My study of the literature is not yet complete. As I stated before, I have found examples of permanent cures of round-celled and spindle-celled sarcoma without the use of the toxin. This paper will be published in a few months, and I shall be able next year to give the comparative results. In my own experience I have never observed a cure in the more malignant forms of the periosteal and medullary sarcoma.

The third paper presented before the Orthopedic Association was by myself. In this I attempted to describe the bone tumors which are curable and in which a cure, as rule, can be accomplished without mutilation. The following is a short abstract of that paper, and if this is read in connection with what I have already published in the December numbers of *PROGRESSIVE MEDICINE*, since 1899, it will be clearer and of greater interest:

The object in the treatment of a bone sarcoma is to insure, if possible, a permanent cure. Amputation is a mutilating operation. The question naturally arises: Can some bone tumors be completely removed without amputation and with the same assurance of a permanent result?

From a personal study, now extending over a number of years, of cases treated in Dr. Halsted's surgical clinic at the Johns Hopkins Hospital, and those in my own practice, and quite a number communicated to me through the courtesy of colleagues, and from the literature, I have found that, with rare exceptions, the permanently cured patients suffered from tumors of similar pathological anatomy, and such cures were accomplished in properly selected cases by conservative operations just as well as by amputation. In that class of cases, in which cures were not accomplished, the pathology of the tumor is very much alike and entirely different from that in the first group. In this latter group, in spite of amputation at the highest joint, patients succumb to internal metastasis.

I shall discuss, first, bone tumors for which the extent of the operation is governed by the local growth, and for which amputation is indicated only when the necessary local resection would leave a limb without function. When amputation is demanded by the local growth of the tumor the highest point need not be selected.

**BONE CYSTS.** There are two varieties. The first, the dentigerous cyst, occurs in the jaws. Undoubtedly it arises from an embryonic residue, mesoblastic or epiblastic, of the dental tissue. This cyst originates within the bony cavity of the upper or lower jaw, and in its growth expands the bone, producing a solid tumor with a bony capsule. This is thin in places and may give rise to parchment or ping-pong-ball crepitation. This cyst can be recognized only at the exploratory incision.

The soft parts are normal; the periosteum, as a rule, strips back easily; the thin shell of bone is uninfiltated. As this piece of bone is removed a thin connective-tissue capsule is exposed composed of an outer layer of dense, white, fibrous tissue which strips from the bone more readily than the periosteum. On the inner surface of this fibrous tissue there is a thin (5 mm.) layer of reddish, vascular tissue. The contents of the cyst are usually clear, viscid serum. In the majority of my cases I have found no epithelial lining; in two the cyst was lined with adamantine epithelium, and the fluid in these two cases resembled that of an atheromatous cyst of the neck. These cysts may be multilocular. In order to accomplish a cure it is simply necessary to remove the membranous lining. The amount of bone capsule to be excised should be governed by the extent of the deformity; resection of the jaw is never indicated.

The second variety of bone cysts occurs in the medullary cavity of the long pipe bones, rarely in the short and the flat bones. It differs from the dentigerous cysts in the absence of a connective-tissue capsule. The fluid is usually hemorrhagic. Islands of cartilage may be found in the bone capsule. Clinically, there is a uniform expansion of the shaft, usually near the joint end, of slow growth. Fracture may be the symptom of onset. Union may take place, but the swelling does not disappear. The x-ray shadow does not differ from that seen in any medullary tumor which produces in its growth bone absorption and retains a bony capsule. The benign nature of the lesion can only be determined with certainty at the exploratory incision. Curetting and drainage of the cyst will accomplish a cure.

**THE ADAMANTINE EPITHELIOMA.** This cannot be distinguished clinically from the dentigerous cyst when it arises within the bony cavity of the jaw, nor from the so-called epulis, when it begins beneath the mucous membrane of the alveolar border of the jaw. At the exploratory incision the adamantine epithelioma can be distinguished from the dentigerous cyst by the coarse, white, granular tissue filling the single or multiple cavities. This tumor must be completely excised with its bony wall, but in the excision one can keep close to the tumor. I have never observed metastasis, and all my observations have remained permanently cured. Further study may demonstrate that in the early stage this tumor may be curetted with the preservation of part of the bony capsule, or one may practise subperiosteal resection and thus limit the mutilation of the operation. When the adamantine epithelioma occurs as an epulis, local removal, with excision of the alveolar border of the jaw only, is necessary. As this is the accepted operation in all pathological varieties of epulides, a differential diagnosis from the latter is not necessary.

**MEDULLARY FIBROMA.** This rare condition may be looked upon as a solid bone cyst, because there seems to be a definite relation between the two. Both may have the same origin; in one liquefaction predomi-

nates, in the other fibrous tissue—ostitis fibrosa. I have tissue from two cases. It is not a malignant tumor, and a conservative operation is sufficient.

**GIANT-CELLED SARCOMA.** This tumor usually originates in the medullary cavity of the long pipe bones, although periosteal growths have been recorded. It is the most common form of epulis which may be looked upon as a periosteal growth from the alveolar border of the jaw. However, I have observed two cases in which the tumor was a medullary growth in the lower jaw.

This tumor has a characteristic appearance in the fresh state. When first seen at the exploratory incision it strikes one by its very hemorrhagic mottled coloring. The majority of areas are red, with here and there specks or smaller masses of pinkish white. The tumor is friable and can be broken up into irregular masses. At first sight it resembles hemorrhagic granulation tissue, but it is firmer and less succulent.

When the giant-celled tumor occurs on a medullary growth it expands the bone like the cyst just described. It may be as slow of growth as the cyst. The *x*-ray shadow does not distinguish it positively from any other medullary tumor having a bone shell. This tumor has been permanently cured by simple curetting. Recurrences have followed curetting, but were permanently eradicated by a second operation of curetting, resection, or amputation. In my investigation of over 100 cases of the pure tumor none have given metastasis. It seems justifiable, therefore, at the first operation to attempt the most conservative method, even with the risk of a local recurrence, which, if it does occur, apparently is not associated with any greater danger of metastasis.

One should not attempt curetting unless there is a thick shell of bone, so that the curette or chisel removes a zone of bone beyond the tumor. When the shell of bone is thin, subperiosteal resection should be performed. When the periosteum and surrounding muscles have become infiltrated, total resection. In one of my recorded cured cases, which had infiltrated muscle, the microscope demonstrated the giant-celled tumor within a few millimeters of the plane of resection.

For the periosteal giant-celled tumor local resection with chiselling of a zone of bone beneath is sufficient.

To one not familiar with the fresh appearance of this giant-celled tumor a rapidly frozen section will be of great value for diagnosis.

As this tumor is relatively frequent, and as in this country amputation has been the method of choice, a knowledge of its characteristic appearances should be acquired by surgeons who desire to cure bone tumors with the least mutilation compatible with absolute safety.

**PURE MYXOMA** is a very rare tumor. It may occur as a medullary growth or a periosteal exostosis. In the former it is connected with the bone shell, in the latter with a partial bony wall. I have observed but one case, a patient of Dr. Halsted's. The myxomatous appearance

of the tissue was sufficiently characteristic to allow a diagnosis. This tumor should be subjected to the same treatment just discussed for giant-celled sarcoma.

**PURE ENCHONDROMA** is not difficult to recognize; it is benign, and local resection is sufficient.

**MYXOCHONDROSARCOMA.** The cartilaginous and myxomatous tumors usually occur together and most often with sarcomatous degeneration. I have been surprised, however, at the excellent results after complete removal. Metastasis is rare, but possible. Curetting should never be employed, but local resection is justifiable. This tumor is very common in the antrum of the upper jaw.

**THE PERIOSTEAL OSTEOSARCOMA.** I am of the opinion that the term osteosarcoma should be given only to that bone tumor associated with new-bone formation. As a matter of fact, this is observed, to any extent, only in the periosteal tumor.

This sarcoma of bone, characterized by spicules of new-bone formation radiating from the shaft between which tumor tissue is present, occurs most commonly on the lower jaw. In my experience none of the cases have given metastasis. Local resection should be the operation. The tumor has a distinct capsule and does not infiltrate the surrounding muscles; it must, however, be removed with the shaft of bone which it surrounds.

At first sight it might seem difficult to differentiate in the *x*-ray picture the following periosteal lesions: ossifying periostitis; osteoma and exostosis; ossifying myositis and periosteal osteosarcoma. Time prevents a detailed discussion here, but the *x*-ray shadows of these diseases are, as a rule, sufficiently characteristic to at least distinguish the benign from the malignant lesion, and the tissues exposed at the exploratory incision are of sufficient difference to confirm the impression gained from the *x*-rays.

**THE PERIOSTEAL FIBROMA.** I have observed this only on the jaw. Local excision is sufficient, even when the tumor has become a fibro-spindle-celled fibrosarcoma.

**EXOSTOSIS BURSATA.** This benign lesion may clinically resemble a rapidly growing sarcoma. The congenital small exostosis springing from the outer table of the bone gives no symptoms. The first rapid swelling observed by the patient is due to the filling of the bursal sac with fluid. We have clinically a rapidly growing tense tumor apparently of periosteal origin. Unless *x*-rays are taken from several views the exostosis may be missed. This lesion is recognized at once if an exploratory incision is made. In one of my cases the patient was sent to me for an inoperable sarcoma of the upper end of the femur over the trochanter, and I must confess, after a careful study of the case, that this diagnosis seemed plausible. The patient's consent to a hip-joint amputation was obtained. Fortunately I followed my rule never to amputate with-

out some positive assurance of the nature of the tumor, and for this reason I made an exploratory incision. There was a distinct sac with a hemorrhagic lining, bloody contents, and, springing from the trochanter, an exostosis with a cartilage cover.

**OSTEOPERIOSTEAL LIPOMA.** A lipoma springing from the periosteum and simulating a periosteal growth is possible. Its nature is of course recognized the moment the tumor is explored. The literature on this subject has recently been collected by Schwarz and Chevrier.<sup>1</sup>

The more malignant sarcomas of bone are rarely permanently cured in spite of the highest amputation performed in many instances a few weeks after the first symptom. Death is due to metastasis, usually to the lungs. The entire duration of life is seldom over two years. I have never observed a permanently cured case. In the literature there are a few, and it is very suggestive that among this group of tumors more cures have been accomplished by local resection than amputation. It is true that, naturally, local resection was selected because of the smaller and more circumscribed character of the tumor. Even in this group, therefore, local resection is justifiable in the early stage of the neoplasm.

These more malignant sarcomas consist of various forms of the round-celled and spindle-celled tumor and the angiosarcoma, chiefly the perithelial.

The medullary growth eats its way through the cortical bone and does not produce bone expansion. Pathological fracture may be the symptom of onset. The periosteal tumor also rapidly infiltrates the cortical bone beneath. In both the character of the tumor tissue is so different from the neoplasms previously discussed that there should be no difficulty in making a differential diagnosis. This diagnosis is suggested by the evidence of bone destruction in the *x*-rays.

Before summing up, I wish to call attention to the importance of an examination of the urine in all cases of bone tumors. In the multiple myeloma of bone Bence-Jones bodies are present. Clinically, this hopeless disease of medullary tissue may, in a few instances, present itself clinically as a single bone lesion. In this stage even *x*-ray studies of other bones may fail to show any other lesion. If the urine is not examined the surgeon would proceed to a radical operation upon the apparent single bone lesion without any suspicion of its multiple nature.

The medullary growth of the myeloma in its early stage expands bone and resembles the giant-celled sarcoma or bone cyst. Later the bone capsule is destroyed. It is important to remember that in some instances the benign bone cyst may be a multiple lesion. The cases thus far recorded have been associated with osteomalacia. Multiple giant-celled tumors have been observed in *ostitis deformans* by Rehn and others.

Fig. 25 represents the second example of pure myxoma recorded in the surgical pathological laboratory. As shown in Fig. 26 it surrounds

<sup>1</sup> *Révue de Chir.*, 1906, xxxiii, p. 469.

the os calcis and is apparently of periosteal origin; the bone is but slightly infiltrated. The patient was a male, aged fifty-six years; a small tumor had been present twenty-five years; three years ago it began to grow, was partially excised, and recurred. Amputation was performed



FIG. 25



FIG. 26

in this case, because complete excision of the tumor would have left a useless foot. Nevertheless, I should have been pleased with an opportunity to attempt a new osteoplastic resection just published by Goldammer<sup>1</sup> the result of which is shown in Fig. 27.

<sup>1</sup> Beiträge z. klin. Chir., 1907, lv, p. 293.

Myxoma is very apt to recur locally whether it arise in bone, soft parts, or, as I have observed it, in the intracanalicular myxoma of the breast. I do not believe, however, that it is a true local recurrence, but take



FIG. 27

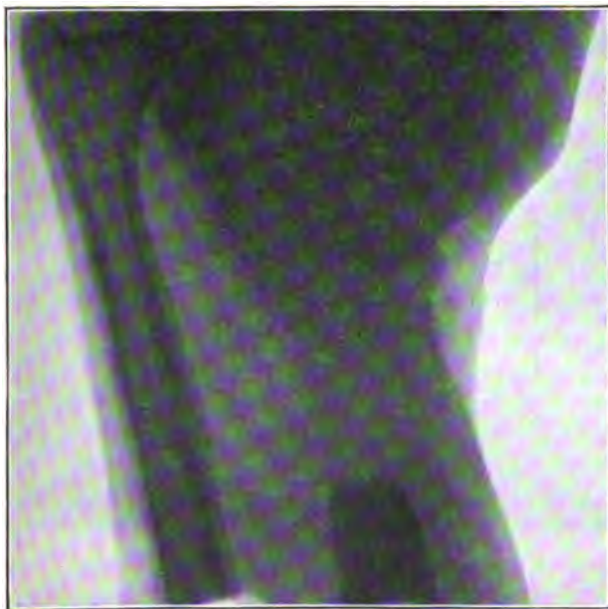


FIG. 28

Borrmann's view that it is autochthonic (regionary) recurrence. That is, myxomas are very apt to be multiple. One of the embryonic areas of cells grows, produces a tumor; this is removed; then a second neigh-

boring area may take on growth, which gives rise to a tumor suggesting regenerative recurrence. In a pure myxoma which I<sup>1</sup> have reported there has been a second operation for a similar tumor in the medullary cavity.

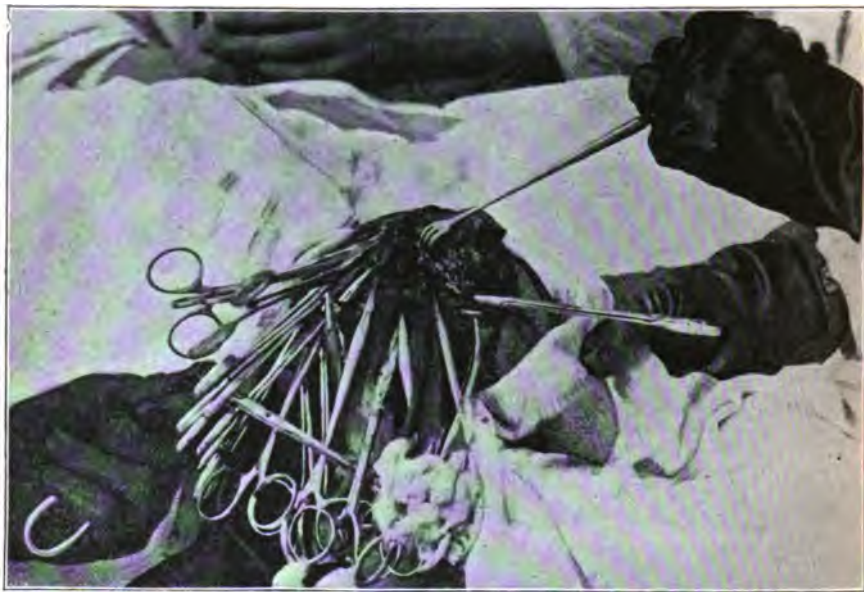


FIG. 29

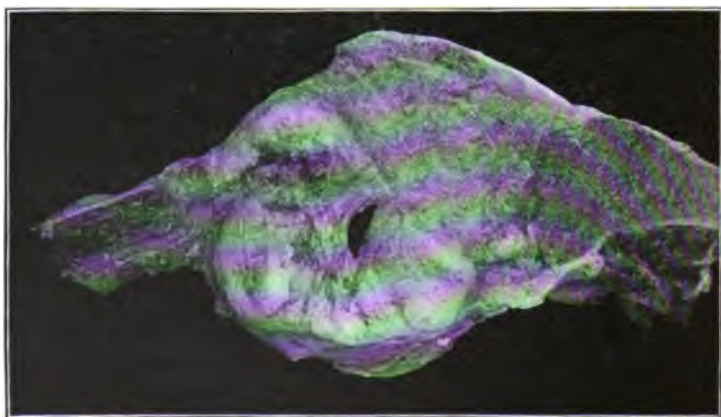


FIG. 30

**GIANT-CELLED SARCOMA.** Whether giant-celled sarcoma occurs as a periosteal or a medullary growth, it is always a cellular tumor, very hemorrhagic, and must be distinguished from the more malignant cellular sarcoma.

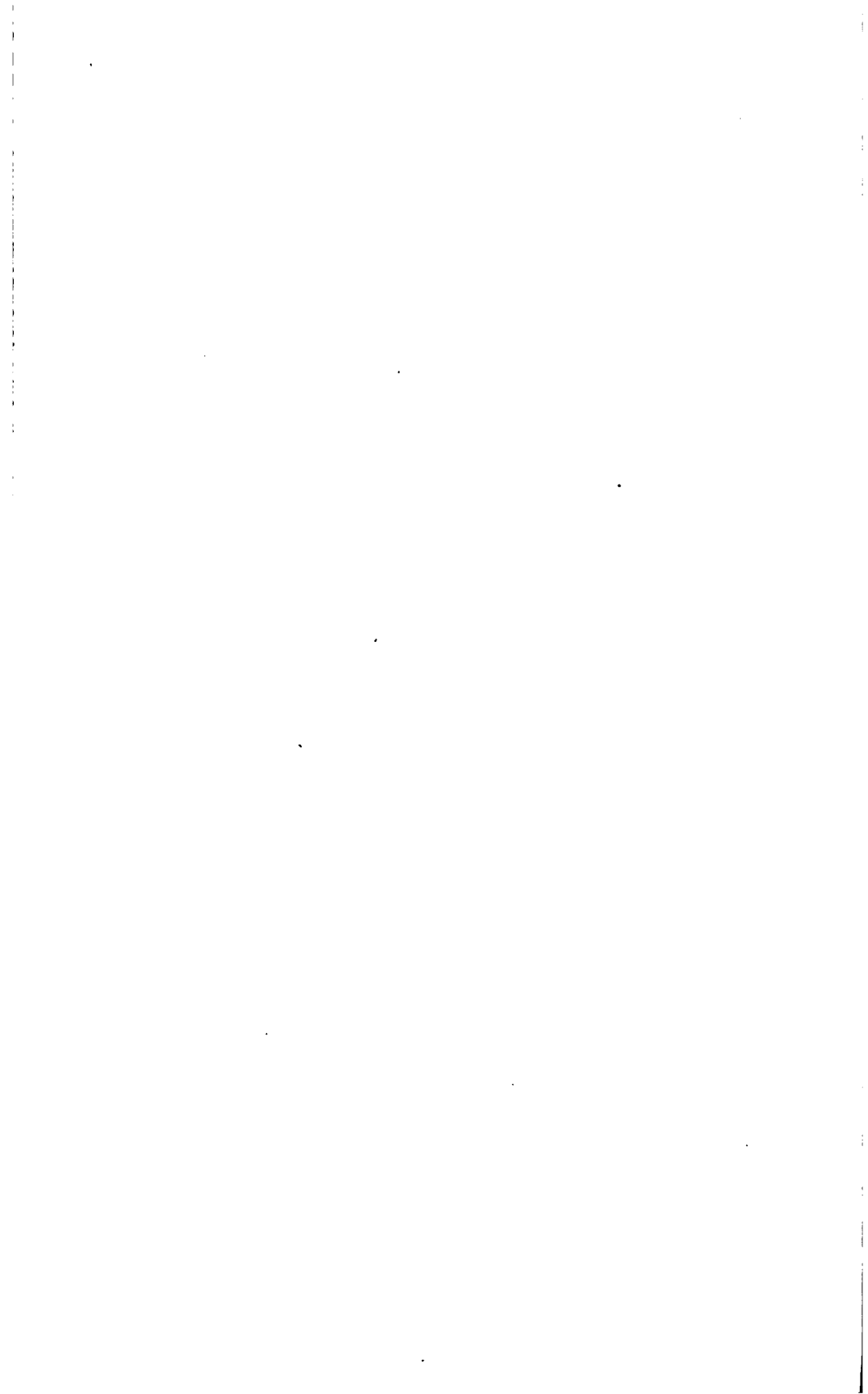
<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906, p. 222, Fig. 19.



A male, aged twenty-nine years, had a tumor at the lower end of the radius, which was first observed twenty months ago after injury; there had been three previous operations: two incisions and curetting, and the last, six months ago, a resection of the lower end of the radius, which is shown in the *x*-ray (Fig. 28). The tumor does not show in the *x*-ray. Notwithstanding the three operations, the local, recurrent tumor had a distinct fibrous capsule and was situated between the extensor tendons and the interosseous membrane; it was easily removed by resection (Fig. 29). In this case the recurrent tumor was not adherent to either ulna or radius.

Fig. 30 is a sagittal section through the lower end of the femur, knee-joint, and tibia in a case of medullary sarcoma which has destroyed the lower end of the femur, completely infiltrated the knee-joint, partly destroyed the articular cartilage of the tibia, and has begun to infiltrate the patella at *x*. At first sight this looks like a very malignant tumor, and might be recorded as a spindle-celled and round-celled sarcoma. Yet I believe the chances for a permanent cure are good, because, histologically, although there are spindle and round cells, the greater part of the tumor consists of fibrous tissue and the spindle cells are producing fibroblasts. The round cells are about areas of hemorrhage and may not be tumor cells at all. In the periphery of the tumor there are osteoblasts and giant cells and here and there cartilage. Unless such a tumor is carefully studied, microscopically, in all its areas, it might easily be recorded as a spindle-celled sarcoma, and if cured, with or without toxins, by amputation or resection, be cited as an example of a permanent cure of a very malignant sarcoma.

The literature during the past year on bone cysts and osteitis fibrosa is so immense that, although I have carefully followed it, I have not space enough to consider the subject farther this year. I am about to publish a monograph with the report of a number of cases, with this literature, and this will allow me next year to continue the discussion of this most interesting bone disease of which, up to the present time, there is very little in English and American literature.



## GENITO-URINARY DISEASES.

BY WILLIAM T. BELFIELD, M.D.

**The Kidney.** HEMATURIA is usually indicative of some gross lesion of the kidney, as traumatism, calculus, tuberculosis, malignant growth, or congestion. It is also well recognized at present that renal bleeding may occur not only in acute nephritis, but also in the chronic forms of nephritis. In addition to these causes bleeding from the kidney occasionally occurs without any adequate explanation; several instances of this character have been recorded during the past year. When bloody urine occurs the question arises, What is the source of the bleeding? Generally speaking it may be said that when the hemorrhage is from the urethra the first urine is bloody and later is clear; when from the bladder the urine may be clear or slightly tinged at first and become increasingly darker; when the source of the bleeding is from the kidney the urine is, as a rule, uniformly colored throughout the micturition.

The recognition of the source of bloody urine, however, is not always so simple a matter, as can be seen by a case reported by Chute.<sup>1</sup>

A woman, aged thirty years, began to have pain in the left costovertebral angle ten years prior to the time of the report. Six months later hematuria first appeared and recurred at intervals for a year. For six months prior to operation the hematuria had become constant and the pain in the left loin more severe. The presence of a palpable and tender left kidney in association with pain in the loin and hematuria naturally suggested that the source of the bleeding was in this kidney. Cystoscopy, however, revealed the fact that the bleeding came from a pedunculated papilloma attached just to the outside of the left ureteric orifice. The removal of the growth gave entire relief. The pain and tenderness were caused by the partial occlusion of the ureteric orifice due to dragging by the growth. This case emphasizes that, after all, the only reliable means of differentiating hemorrhage from the bladder or kidney is by direct inspection. Segregators would have led to faulty conclusion in this instance.

Another case illustrating how faulty conclusions may be drawn as to the source of the bleeding is reported by Young.<sup>2</sup> In this case there had been persistent hematuria for sixteen months, the hematuria developing ten days after a traumatism to the left side. Young states the case

<sup>1</sup> Journal of Urology, January, 1907.

<sup>2</sup> Journal of American Medical Association, May 18, 1907.

is of special interest in that the pain was constantly present in the side injured, but the hemorrhage came from the opposite side; because of the absence of any signs of nephritis, which is held to be generally present in such cases; and because no previous publication of the use of *adrenalin* for such purpose has been found in the literature.

It is noteworthy that some hours after the injection of adrenalin the patient had several distinct attacks of renal colic, with the passage of blood clots, and that blood persisted in the urine for ten days thereafter. It may, therefore, be debated whether the arrest of the hematuria was due to the injection of adrenalin or to the passage of irritating concretions out of the kidney. Reference is made to Fowler's<sup>1</sup> case of unilateral hematuria. In this instance a microscopic examination of the removed kidney showed a diffuse chronic nephritis. An increasing amount of albumin and casts with, later, the presence of a few red blood cells made it apparent that the supposedly sound kidney was also diseased. A careful study of the literature by Fowler showed that many of the instances of hematuria from sound kidneys were really cases of nephritis. He quotes Schede, however, as saying that he has found six cases recorded by competent observers in which a careful examination of the kidneys failed to show any cause for the hematuria.

Casper<sup>2</sup> records two cases in which a careful macroscopic and microscopic examination failed to show the source of the hemorrhage. With the exception of a few small fibrous points the kidneys were normal. The significance of these fibrous foci will be considered farther on. Casper, in addition, reports four instances of hematuria due to chronic parenchymatous nephritis and one due to carcinoma involving the pelvis of the kidney.

Cumston<sup>3</sup> summarizes our knowledge of hematuria from renal lesions, emphasizing the presence of local foci of sclerosis as the source of persistent bleeding for years. He states that in descending or hematogenic nephritis the renal gland gives evidence, in the very acute forms, of violent congestion, occasionally with ecchymoses, hemorrhages, and slightly evident epithelial lesions. In the acute forms one may meet with the same lesions as in the very acute form, but with a hemorrhagic predominance. The prolonged types with the elimination of bacteria and their toxins finally end in sclerotic lesions due to the reaction of the connective tissue, which in their turn cause the kidney to bleed. Bright's disease may be the cause of slight, severe, or persistent bleeding. Here the bleeding is believed to be due to congestive attacks, aided by disturbances of innervation, changes in the blood and vascular lesions, all of which favor hemorrhagic rupture. Generalized arterial hypertension and cardiac hypertrophy, so frequently associated with the small, contracted kidney, are believed by Pousson to favor rupture of the vessels.

<sup>1</sup> Johns Hopkins Hospital Reports, vol. xiii.

<sup>2</sup> Quoted by Young.

<sup>3</sup> Journal of Urology, May, 1907

Cumston draws particular attention to another form of nephritis which plays a very important part in the pathogenesis of hematuria. These nephritides manifest themselves clinically only by hematuria and occasionally by albuminuria and pain. The sclerotic lesions met with in these cases present certain peculiarities, for they are, in the first place, and for a certain time, unilateral, afterward becoming disseminated in the midst of healthy tissue to more or less extent. These lesions, although frequently microscopic, are termed by Cumston *partial nephritis*. This form may give rise to formidable hemorrhage. Instances of so-called "essential hematuria" doubtless, in many cases, belong to this group. The view that nephritis may, at times, be unilateral and involve isolated portions of one kidney only, is held by Israel, Pousson, Edebohls, Rovsing, and others.

Cumston states that the nature of these lesions readily explains the mechanism of the hemorrhage, which, as in Bright's disease, is dependent upon disturbances of the innervation, blood changes, and vascular lesions. Under ordinary circumstances the circulation may still be carried out effectively, even in this vascular system so markedly changed, but the slightest disturbance causes trouble. Thus attacks of congestion end all the more easily in a hemorrhagic rupture, the more fragile the vessel walls have become by arterial sclerosis.

Chute<sup>1</sup> states that the hematurias due to chronic nephritis differ from those arising from acute nephritis in that they last longer and are often profuse. The bleeding is usually intermittent and may extend over a very long period (two years and a half, Keersmaecker). It may, on the other hand, be continuous and moderately profuse, as in a case Chute himself reported. Hematuria due to *renal tuberculosis* is generally met with in early adult life, though, as Chute<sup>2</sup> states, it is by no means restricted to this period. The bleeding in these cases, while usually small in amount and intermittent, may occasionally be profuse and continuous. In addition to blood the urine in these cases will show a greater or lesser amount of pus and pelvic epithelium. The presence of a thickened ureter on the bleeding side is highly suggestive of tuberculosis, as are ulcers or a localized cystitis about the ureteric orifice of the same side. The real test of the nature of the condition is the finding of tubercle bacilli in the urinary sediment or the production of tuberculosis in guinea-pigs by inoculation of this sediment. Cases of renal tuberculosis which are most confusing are those in which there are small, well-walled foci of tuberculosis deep in the substance of the pyramid, with no connection with the renal pelvis. Hematuria may occur in these cases as a result of congestion or interference with the renal circulation. The demonstration of tubercle bacilli in these cases is difficult.

Meyer records an instance of severe hematuria following medicinal doses of chlorate of potassium.

<sup>1</sup> Loc. cit.

<sup>2</sup> Loc. cit.

**PAIN IN RENAL AND APPENDICULAR AFFECTIONS.** Schlesinger<sup>1</sup> cites instances from Israel's surgical clinic in which considerable difficulty was encountered in differentiating between appendicitis and trouble in the kidney or ureter. He states that he has observed red blood cells in the urine of individuals suffering from appendicitis, although Tuffier claims that blood cells are always indicative of nephritis. On the other hand, the existence of a nephritis is sometimes masked by intestinal phenomena.

The following cases illustrate the difficulties encountered: A man had had recurring attacks of pain, believed to be due to appendicitis, for eight years. The attacks began with pain in the penis and right buttock, painful urination, and tenesmus. As the pain increased there was retention of both urine and feces, with marked abdominal pain extending to the right lumbar region and hip. Vomiting also occurred. After the patient was able to urinate the pain ceased. These attacks lasted from four to ten hours. Following the last attack the pain extended to the right costal arch and there were "stitches" in the right leg. Those who examined the man differed as to whether he had appendicitis or some nervous affection. Israel was of the opinion that he had a stone in the right ureter. Both the x-rays and operation confirmed this diagnosis. In regard to the pain in the buttock and penis, Israel states that this distribution is always due to extraperitoneal causes. While chronic appendicitis may cause disturbances in urination, they are never so marked as in the case just cited. In another case with pain in the ileocecal region radiating into the testicles and painful urination, an appendectomy was done. A few months later the patient had an unmistakable attack of renal colic, with the passage of a stone. In a third case cited by Israel there was renal colic (irritation of the bladder and radiation of pain to the testicles) accompanied by obstipation and vomiting. In this instance an artificial anus was made.

*Spermatic Colic.*<sup>2</sup> The spasmodic and exquisitely painful contractions of an infected seminal vesicle has been repeatedly mistaken both for appendicitis and renal colic. In one case that I treated by injecting the vesicle from the vas deferens, the patient had some time before submitted to appendectomy without relief from recurring attacks of pain. In several cases of recurrent spermatic colic, operation for ureteral calculus had been urged.

*Renal Colic due to an Anomalous Artery.* Ekehorn<sup>3</sup> reports a woman who had suffered for six years with recurring attacks of colic in the right kidney. Since her last pregnancy the condition had become worse. At operation the only cause of the trouble to be found was an accessory artery entering at about the centre of the lower half of the kidney. The

<sup>1</sup> Deutsch. med. Wochenschrift, 1906, Nr. 44.

<sup>2</sup> Trans. Amer. Assoc. Genito-urinary Surgeons, 1907.

<sup>3</sup> Archiv f. klin. Chirurgie, Band lxxxii, Nr. 4.

ureter had to turn back on itself to pass over this artery. The artery was severed and ligated; complete relief of the symptoms followed the operation. Ekehorn found 24 somewhat similar cases in the literature. These anomalies are very apt to cause disturbances, especially if the organ becomes even slightly displaced.

*Congenital Transposition of the Kidney.* Gronnerud and Parkes<sup>1</sup> describe and picture this renal abnormality, which illustrates one source of uncertainty in surgical procedures on the kidneys. Even catheterization of the ureter might fail to arouse the operator's suspicion as to the existence of an abnormality, unless x-ray pictures were taken of the ureter catheters *in situ*.

In this case the right kidney was found on the left side of the vertebræ, in immediate contact though independent of the left kidney, only the fatty and fibrous capsules being common to both. Although misplaced, the bloodvessels of this kidney arose, as though it were properly placed, from the normal level and side of the aorta and vena cava. The ureter also entered the bladder normally. The left kidney was normally situated, except that it was somewhat lower than is ordinarily the case. The ureteral orifice on the left side was considerably higher than on the right—due, the authors believe, to traction. The mass showed that there were two distinct pelves with the vessels relatively distributed.

**TOXIC NEPHRITIS CAUSED BY SURGICAL LESIONS.** Jacobson<sup>2</sup> calls attention to the fact that surgical conditions that are capable of producing pathological conditions in the kidneys have not received much study. He states that it is quite commonly held that the presence of a nephritis is a possible contra-indication to a surgical operation. He believes, however, that in a certain class of cases bacterial or toxic nephritis becomes a very positive indication for operation, as it is only in this way that the nephritis can be removed. Jacobson states that the question arises whether this form of nephritis is due to the bacteria or the toxins produced by them. From a review of the experimental work done it seems that in cases of general infection the passage of bacteria through the kidneys is capable of producing various anatomical and pathological changes in the kidney structure. Jacobson cites three cases: one with septic endocarditis as well as nephritis, probably due to a staphylococcic infection; another with intestinal obstruction which awakened a serious and almost fatal nephritis, and a third case with gallstone disease and subacute pancreatitis, giving rise not only to nephritis, but also glycosuria. In each of these cases removal of the exciting cause relieved the nephritis.

**The Ureter.** URETERAL OCCLUSIONS, according to Beer,<sup>3</sup> cannot be accurately determined by cystoscopy; neither can reliable information be obtained by either ureteral catheterization or the indigo-carmin test

<sup>1</sup> Journal of the American Medical Association, August 24, 1907.

<sup>2</sup> Ibid., March 3, 1907.

<sup>3</sup> Annals of Surgery, October, 1906.

alone. He has found, however, that by combining ureteral catheterization and the indigo-carmin test the presence or absence of obstruction as well as the degree of patency of the ureter can be satisfactorily determined.

IMPLANTATION OF THE URETER IN THE BLADDER has been successfully done by Franz<sup>1</sup> in fifteen cases. The transplantation was usually done because of injury to the ureter in extensive abdominal operations. The results, both immediate and remote, were extremely satisfactory in most of the cases and did no harm in any instance. In two of his cases it was impossible to effect transplantation and the kidney had to be removed.

Franz found that to obtain satisfactory results it was necessary to avoid crushing the ureter at any point and to use as little suture material as possible.

THE URACHUS. In PROGRESSIVE MEDICINE for June, 1907, p. 67, Foote reviewed several articles on *cysts of the urachus*. Weiser<sup>2</sup> gives a summary of 89 cases; of this number more than two-thirds occurred in females. MacDonald<sup>3</sup> has recently observed a case. The patient, aged forty, gave a history of a slowly growing abdominal tumor, beginning in the region of the bladder and growing upward. With the gradual increase in the size of the tumor pressure symptoms became marked, especially difficult respiration, pain, and impaired indigestion. At operation the tumor was found to be in front of the peritoneum and surrounded by very firm adhesions which were broken up with great difficulty. The wall of the cyst contained a number of nodules which proved to be papillomas. In spite of an infection with the colon bacillus the patient made a satisfactory recovery.

Fanoni<sup>4</sup> reports a case of *intestinal obstruction due to a persistent urachus*. The urachus was about the size of the little finger and was attached at its lower end to the fundus of the bladder and at the upper to the anterior abdominal wall, one inch above and two inches to the right of the umbilicus. The upper end divided into three branches, spreading out in the shape of a fan. There was no connection with the liver. The obstruction was caused by a portion of the intestine becoming caught between the urachus and the abdominal wall. The constriction was relieved by ligating the urachus at both ends and its side. The patient made a good recovery, but two months later complained of cramp-like pains in the abdomen and constipation. Examination of the abdomen showed a swelling over the site of the stump of the urachus, which had been left. On making an incision over this swelling and through the structures down to the peritoneum some cheesy material was found and removed. The three remnants of the roots of the urachus were also removed. A loop of intestine had become constricted as the result of

<sup>1</sup> Zeitschrift f. Geb. u. Gyn., 1907, Nr. 1.

<sup>2</sup> Annals of Surgery, August, 1907.

<sup>3</sup> Quoted by Foote.

<sup>4</sup> Post-Graduate, July, 1907.



adhesions between the omentum and stump of the urachus. A lateral anastomosis was done and the patient made a good recovery.

There was no evidence of tuberculosis in either the intestines of the peritoneum.

**The Bladder.** **SIMPLE ULCER OF THE BLADDER.** The bladder, like that other hollow organ whose mucous surface is regularly bathed in an acid liquid, the stomach, presents an ulcer called "simple"—*i. e.*, of unknown etiology—to distinguish it from ulcers of known cause, such as the tuberculous and malignant ulcers. The simple ulcer of the bladder is commonly described as a rare lesion, though this may be interpreted as meaning that the ulcer is rarely recognized clinically. It is discovered during life only through the cystoscope, and the more general employment of this invaluable instrument is increasing the number of cases in which "simple" ulcer of the bladder has been identified.

Walker<sup>1</sup> describes two cases personally observed, in which improvement of symptoms occurred under injections of *silver nitrate* solution, 1 to 10,000, and gives a summary of our present knowledge of the lesion.

He states that the three prominent symptoms are increased frequency of micturition, pain in the penile portion of the urethra, and hemorrhage.

The first stage is characterized, as a rule, by some disturbance of micturition, the act being more frequent and the passage of the urine attended by a burning sensation, particularly marked toward the end. Not infrequently more or less discomfort is felt in the penis. The urine does not show any very marked change, but close examination will show some pus, necrotic debris, and exfoliated epithelium.

Later, when the second stage develops, cystitis appears and all of the above symptoms are exaggerated. Micturition is more frequent and painful, and there is a sensation of not being relieved until several minutes after the act is finished. Discomfort in the suprapubic and perineal regions is more or less continuous, while the pain in the penile urethra increases and is sometimes extremely severe.

The urine in this stage is more purulent and contains more epithelium and debris; blood also occurs in larger amount.

In the third stage the bladder loses its expulsive power and the patient is unable entirely to empty it. In this stage calculi may form, and these, together with the purulent urine, greatly aggravate all the symptoms. Walker states that if the patient is not now relieved he will die from exhaustion or from an ascending renal infection.

In another type, the *acute perforating ulcer*, there are no symptoms whatever until perforation has taken place. In such instances blood usually appears in the urine in either small or large amounts, and in a few hours signs of perforation are present.

Walker quotes several instances of this accident from the literature.

<sup>1</sup> Journal of the American Medical Association, March 23, 1907.

In these cases there was usually a history of perfect health up to the time of the perforation. The patient will suddenly experience acute pain in the lumbar region, groin, or perineum. Bloody urine may not appear for forty-eight hours, but, as a rule, it appears very shortly after the perforation and may be quite profuse. The patient may live without operation for five days or die in thirty-six hours, as in the case observed by Pousson. Of the 6 cases cited by Walker, perforation occurred in the posterior wall in 4, at the summit in 1, and in 1 the location is not mentioned.

*The Diagnosis* of simple ulcer in the earlier stage is possible by the cystoscope only. The ulcer has a punched-out appearance, with clean, smoothly cut, and slightly indurated edges. The remainder of the mucosa is normal. A simple ulcer is differentiated from a tuberculous ulcer by the regularity of its edges, the appearance of its base, the absence of undermining of the margins, of surrounding tubercles, and of tuberculosis in other organs.

In the later stages the cystoscopic appearances and the local symptoms are very similar to those of tuberculous ulcer of the bladder. It is quite possible that the simple and the tuberculous ulcer have often been mistaken one for the other; that many cases in which ulcers have been recognized by the cystoscope, and smegma bacilli found in the urine have been mistaken for tubercle bacilli, have been called tuberculous though really simple ulcers. Possibly some of these have been healed under treatment and recorded as cases of healed tuberculous ulcers.

Our literature of bladder ulcers needs careful revision as our acquaintance with the "simple" ulcer improves.

*Prognosis.* Walker states that in the earlier stage of simple ulcer the prognosis is good under proper treatment. In the second stage, when lime salts have been deposited and the ulceration has increased, curetting and drainage will usually effect a cure. In the third stage, with interstitial changes, the prognosis is very grave. Patients who have reached this stage usually die either from exhaustion, an ascending infection, or other complication.

The acute perforating type is usually fatal; practically always so when the peritoneum is implicated. Walker was able to find but one instance in which recognition of the perforation and operation had saved the patient.

*Treatment.* In the first stage the most efficient treatment is irrigation with silver nitrate from 1 to 10,000 up to 1 to 5000 every second day. If after a sufficient trial this does not succeed, the ulcer may be cauterized with the cauterizing cystoscope, or a suprapubic opening made and the ulcer curetted and cauterized with the Paquelin instrument.

In the second stage a curetting and cauterization with prolonged drainage through a suprapubic opening are necessary to effect a cure.

In the third stage Walker states that the changes that have taken place render it unlikely that healing can be accomplished. Drainage, irrigation, and gradual distention of the bladder are all that can be done.

**CANCER OF BLADDER.** Cabot<sup>1</sup> reviews a dozen cases of vesical cancer operated on in Boston hospitals, and offers the following conclusions based thereon: (1) That palliative operation is of value in the treatment of cancer of the bladder. (2) That in properly selected cases operation will prolong comfortable existence very materially. (3) That suprapubic drainage of the bladder will relieve the symptoms and promote the comfort of patients for whom nothing more radical can be done. (4) That hemorrhage should not be allowed to continue unchecked unless efficient examination has conclusively shown that its cause cannot be removed by operation.

Kolischer and Schmidt<sup>2</sup> discuss the operative treatment of vesical cancer with more optimism than has usually been expressed by others.<sup>3</sup> They emphasize the comparatively few good results obtained by operation, and suggest that many of the poor results are to be explained by the tardiness in operating. Thus, there are 2 cases of vesical cancer on record in which total extirpation of the bladder accomplished a cure without relapse for five years (Hogge), and for fifteen years (Pawlik), respectively. Rafin reports 5 cases of partial resection of the bladder for carcinoma that remained cured for more than three years. In Czerny's sarcoma case the patient lived for twelve years after the operation without relapse. Quite a few surgeons report cases of malign bladder tumor which, after partial vesical resection, have remained cured for from one to three years.

They offer the following propositions: (1) All benign tumors of the bladder should be approached from the inside, all malign tumors from the outside of the viscus. (2) In all malign cases in which the loss of substance is not too great the bladder should be closed completely by sutures after the removal of the tumor. (3) In cases of malign tumor the incision into the bladder should be made in accordance with the location of the growth, as defined by the cystoscope. (4) The permanent catheter should be absolutely abolished. (5) Gas anesthesia should be employed exclusively. (6) A constant cystoscopic surveillance should be maintained over any bladder that has ever been operated on for tumor.

I have reviewed<sup>4</sup> the hundreds of operations reported by Keydel, Trephin, Watson, and others, which give a vanishingly small percentage of permanent cures. I am inclined to explain these poor results in part by the inherent malignancy of tumors derived from recently specialized epithelium.

The malignancy and frequency of cancer seem to vary directly with the phyletic age of the various organs, being least in the earliest, greatest

<sup>1</sup> *Journal of Urology*, September, 1907.

<sup>2</sup> *Journal of the American Medical Association*, July 27, 1907.

<sup>3</sup> See *PROGRESSIVE MEDICINE*, December, 1906, p. 126.

<sup>4</sup> *Journal of Urology*, May, 1907.

in the latest organs. Thus carcinoma is notoriously frequent and malignant in the breast and the uterus. The breast, a specialized skin gland, appears with the mammals; the completely fused uterus with specialized cervix appears in the apes—both, therefore, among the latest organs. Cancer of the skin in general—that primeval organ—is notoriously benign compared with that of the breast; cancer of the Fallopian tubes and the vagina (ancient parts of the Müllerian duct) is far less malignant and frequent than that of the uterus. Cancer of the rectum, stomach and large intestine is more frequent than in the older small intestines. Of the urinary organs the bladder is the latest, appearing first in the amphibians; and vesical cancer is more frequent and malignant than the same disease in the more ancient ureter and kidney.

The malignancy of bladder cancer may be compared with that of the breast; further experience has corroborated the doubt expressed by Guyon many years ago as to the benignancy of any form of epithelial bladder tumor. The surgery of vesical cancer, which is the creation of the cystoscope and therefore only twenty years old, has taught the same lesson learned through longer experience in the surgery of the breast. At first the surgeon removed cancer from the breast; then he removed the breast with the cancer; and in these latter days he removes the breast and all accessible lymph glands and fasciæ liable to infection. And yet the permanent cures of cancer in this organ—ideally situated for surgical attack—do not average more than 33 per cent.

Still less favorable are the final results in the removal of vesical cancer, more difficult of access than is the breast. At first surgeons removed merely the cancer; then they resected the bladder with the cancer; latterly they have removed the entire bladder—and yet permanent cures are less than 25 per cent.

The potential malignancy of vesical tumors, even of apparently benign papillomas—which has been abundantly shown by clinical experience, seems to be inherent in the bladder epithelium. The most obvious explanation is that which ascribes the especial malignancy of carcinoma in breast, uterus, rectum, and prostate—as well as bladder—to the genetic activity of recently specialized tissues, which may be called the phyletic factor in carcinoma.

**TUBERCULOSIS OF THE BLADDER.** Kümmell<sup>1</sup> states that in women suffering from tuberculous nephritis or cystitis the trouble is frequently referred to the genital organs, and that these patients are treated for uterine displacement or some allied condition. An examination of the urine will, under such circumstances, often give a clue as to the true condition. A chronic gonorrhea in either a man or woman sometimes masks the real trouble. Kümmell urges that in individuals showing some cloudiness of the urine, slight cystic disturbances, especially in

<sup>1</sup> Archiv f. klin. Chirurgie, Band lxxxi, Heft 1.

women, pain in the region of the kidney, with pallor and loss of weight, the urine should be examined for tubercle bacilli.

In an analysis of the cases of tuberculosis of the bladder occurring in the Johns Hopkins Hospital, Walker<sup>1</sup> found no instance of complete recovery.

Tuberculosis of the bladder is, of course, seldom primary, being usually subsequent to, as well as consequent upon, tuberculosis of the kidney or of the genital tract. Others have been more fortunate than Walker, in seeing symptomatic recovery of both urinary and genital tuberculosis with extension to the bladder. Whether such symptomatic recovery is an absolute and permanent cure is not so easily affirmed.

The treatment of genital and urinary tuberculosis by the *new tuberculin*, especially when the dosage is regulated by determining the opsonic index of the patient, has received new impetus through the work of Wright.

Wright cites the case of a man aged twenty, with swelling and tenderness in the prostate and neck of the bladder; the urine contained some blood and large quantities of pus. Tubercle bacilli were found in the urine, and cultural methods showed that there was no other bacterial invasion. This patient had previously been under treatment with new tuberculin, the dose having been gradually increased to  $\frac{1}{2}$  mgm. Larger doses aggravated the bladder symptoms. The dose was then reduced to  $\frac{1}{10}$  mgm. and gradually brought up to  $\frac{1}{5}$  mgm. The opsonic index, taken before the readjustment of the dose, was 0.62; there was no improvement in either the symptoms or the index. The dose was then reduced to  $\frac{1}{8}$  mgm., continued at ten-day intervals for a time, and then increased to  $\frac{1}{4}$  mgm. and later reduced to  $\frac{1}{10}$  mgm. Under these small doses there was marked improvement. Frequency of urination and the prostatic swelling abated and the pain disappeared. The urine could be held for two hours and the patient was less easily fatigued.

Wright is very enthusiastic over the results that may be obtained in cases of localized tuberculosis by means of tuberculin controlled by the opsonic index. He urges that before patients suffering from a localized bacterial infection are turned over to the surgeon they be first subjected to inoculation with the appropriate bacterial vaccine.

Wright's work indicates that we have generally used the new tuberculin in excessive doses, and that our uncertain and contradictory results are to be explained in part by the excessive dosage, in part by our habit of depending upon the "reaction" rather than upon the opsonic index as a guide in treatment.

**TOTAL EXTIRPATION OF THE BLADDER.** Rovsing<sup>2</sup> describes his technique for this operation and reports 3 cases in which satisfactory

<sup>1</sup> Annals of Surgery, April, 1907.

<sup>2</sup> Archiv f. klin. Chirurgie, Band lxxxii, Nr 4.

results were obtained. The abdominal incision is curved, with the convexity down. The bladder is removed entire, just as a cystic tumor is shelled out. If the peritoneum cannot be readily separated it is removed with the bladder. The ureters are ligated about 1 cm. above and divided between two ligatures with a cautery. In women the neck of the bladder and 1 or 2 cm. of the urethra are then severed with a small angiotribe. In men the prostate and bladder must be separated from the rectum before the urethra can be reached and severed. In this way the bladder can be removed in its entirety with little or no hemorrhage. If the peritoneum has been opened it is sutured and the cavity left by the removal of the bladder is lined with gauze and filled with gauze strips, moistened in a 1 or 2 per cent. solution of silver nitrate. The ends of the gauze strips are brought out through the centre of the wound.

The next step in the operation is the disposal of the ureters. For this purpose a short incision is made in the lumbar region on each side, extending from the margin of the erector spinæ outward. The ureters are then hooked up, near the kidney, with the forefinger, gently loosened below, and brought out through the wounds. They are not fastened to the skin, as a funnel-shaped retraction is apt to occur. The ureters are left hanging from the wounds, protected by a glass vessel after a No. 12 rubber catheter has been passed in just beyond the abdominal wall. The projecting part of the ureter is protected by a rubber cot. The exposed end shrivels up for 2 or 3 cm., and by the end of a week, when the wound has healed, the exposed part is cut off, leaving a small projection standing above the skin like a beak-shaped urethra. This outer exposed part soon becomes coated with epidermis. Rovsing has devised a belt which controls the flow of urine. A woman has worn one of these belts for eleven months with perfect satisfaction. In addition to doing away with the danger of infiltration of urine or the contamination of feces, Rovsing claims an additional advantage for this method, namely, that there is no danger of secondary infection such as almost invariably follows transplantation into the vagina or intestine.

Bottomley,<sup>1</sup> after reviewing the various methods practised to secure relief from the distress occasioned by bladder exstrophy, describes an operation which he has successfully practised. He transplants the ureters into the skin of the loin, following the general plan outlined by Rovsing after total extirpation of the bladder.

**RUPTURE OF THE BLADDER** following a severe abdominal injury is reported by Quick.<sup>2</sup> The case is of especial interest in that there was no shock and the man continued at his work, as a laborer, an entire day after the accident. Subsequently he suffered from anuria and progressive distention of the abdomen. He was operated on ten days and a half after the rupture and was discharged cured ten days later.

<sup>1</sup> Journal of the American Medical Association, July 13, 1907.

<sup>2</sup> Annals of Surgery, January, 1907.

An analysis of 23 cases of rupture of the urinary bladder has been made by Besley.<sup>1</sup>

**STONE IN THE BLADDER.** Obstruction of labor due to a bladder stone becoming wedged between the symphysis and head of the child is reported by Wagner.<sup>2</sup> The stone measured 2 x 4 x 6 cm. After the woman had been in labor four days the cause was recognized and reduced under chloroform anesthesia. The woman was then delivered of a macerated child. From this experience and a study of 46 similar instances recorded in the literature Wagner advises removal of the stone before childbirth. Allowing the stone to remain is almost certain to cause injury to the bladder, vagina, or sphincter during labor, to say nothing of offering obstruction to the delivery of the child.

A large *calculus* having as its nucleus a gold ring was removed by Faulds.<sup>3</sup> He cites other cases in which the nucleus was a small silver coin, a small brass bell, pieces of copper, a slate pencil, etc. In all of these cases the presence of a cystitis caused the patients to seek medical advice.

Muren<sup>4</sup> reports 16 cases of bladder stone, in which, with one exception, *litholapaxy* was done without anesthesia. Before attempting this operation Muren states that the general condition of the patient should be improved as much as possible, and that the bladder should be subjected to thorough washings. Some urinary antiseptic should also be given during the preliminary treatment. The crushings were all done in the office.

Fragmentation and removal of the stone may be practised once a week unless some special contra-indication exists.

**THE USE OF OXYGEN FOR CYSTOSCOPY AND RADIOGRAPHY.** In cases where the bladder is irritable Burkhardt<sup>5</sup> has found that it is a great advantage to fill the organ with oxygen, instead of air or fluid, as a preliminary to cystoscopy or radiography. The oxygen, in addition to having a soothing and sedative effect on irritable bladders, possesses the additional advantages of being free from the danger of producing an embolism and permits of a much clearer shadow when a stone is present. In direct inspection of the bladder the oxygen also allows of a much clearer view.

Burkhardt suggests that as the oxygen has proved so successful in the bladder, it might advantageously be introduced into the hilus of the kidney through the ureter catheter in obscure cases of kidney stones.

**The Prostate.** Virghi<sup>6</sup> is of the opinion that *chronic prostatitis* is invariably caused by a mild infection of the prostate with the colon

<sup>1</sup> Surgery, Gynecology, and Obstetrics, April, 1907.

<sup>2</sup> Zeitschrift f. Geb. und Gyn., Band lix, Nr. 2.

<sup>3</sup> Glasgow Medical Journal, January, 1907.

<sup>4</sup> New York State Journal of Medicine, January, 1907.

<sup>5</sup> Münchener med. Wochenschrift, 1907, Nr. 1.

<sup>6</sup> Abstract.

bacillus. In 125 cases of prostatitis, all with gonorrheal antecedents, he found the colon bacillus alone in 60 and in association with other bacteria in 65. In 38 others without gonorrheal antecedents the colon bacillus was present in all but 6. As a result of the chronic inflammation thus produced the prostate enlarges and the only means of arresting it is by massage of the prostate, prostatic urethra, and neck of the bladder.

Goldberg<sup>1</sup> takes an entirely different view, his experience being decidedly against the assumption that the prostate becomes enlarged only as a result of an inflammatory process. While unhealed gonorrhea is an important factor in some cases of enlargement, he does not think the relation between them is, as a rule, as close as is generally thought. Out of 50 patients with enlargement of the prostate, Goldberg obtained a venereal history in only 25 per cent. Occasionally in cases of prostatitis in young men the prostate was altered as in prostatic enlargement, but there were no objective disturbances of enlargement. These cases suffer from neurasthenia and hypochondria.

In a few cases Goldberg found symptoms of actual enlargement, retention of urine, residual urine, secondary infection of the urinary passages, etc. In some the prostate was small, in others moderately enlarged. Goldberg terms this group chronic cystoparetic prostatitis. He believes that many of the cases of "soft enlargement of the prostate" belong to this group, the only difference being that the patients are elderly men. It is important to distinguish between prostatitis and enlargement because of both prognosis and treatment.

The apparent disagreement between the two opinions just quoted arises from Goldberg's failure to recognize, as does Virghi, the existence of two essentially diverse lesions of the prostate in elderly men. This subject was elaborated in *PROGRESSIVE MEDICINE*, December, 1906, p. 142.

**OPERATIVE TREATMENT OF CHRONIC PROSTATITIS.** While massage, sounds, instillations, and hygiene produce the desired results in most cases of chronic prostatitis, there is occasionally found one which proves refractory to such treatment. Some years ago the removal of the prostate by the perineal operation was practised in these cases, but never found favor. Young<sup>2</sup> revives this proposal, and relates 4 cases which he operated with entire satisfaction.

As surgeons have already passed this procedure in review, it is probable that most of them will continue to practise that generally successful method, stretching of the prostate either by a urethral dilator or by the finger introduced through a perineal median incision.

Stokes<sup>3</sup> has in 4 cases added to such stretching the curetting of the prostatic urethra through the perineal incision.

<sup>1</sup> *Zentralblatt f. Chirurgie*, 1907, Nr. 7.

<sup>2</sup> *Urological Studies*, Johns Hopkins Hospital Reports.

<sup>3</sup> *Journal of Urology*, December, 1906.



**RADIOTHERAPY OF THE ENLARGED PROSTATE.** The error of failing to distinguish between inflammatory enlargement of the prostate caused by pus infections and the real adenomatous hypertrophy has resulted in reports of alleged success in treating "prostatic enlargement" by the Röntgen rays.

Haenisch<sup>1</sup> claims to have gotten good results by this method. His technique is as follows: The patient assumes a partial knee-elbow position, the trunk resting on an adjustable cushioned support, and the arms and elbows on a lower cushion. The tube is attached to an adjustable standard and folding arm, the rays being centred in a lead glass speculum fastened in the rectum. The distance between the anticathode and the entrance of the speculum should be about 27 cm. The exposures lasted about six minutes each; 6 or 8 exposures were made in the course of two or three weeks. Haenisch believes that the success of the treatment is in inverse proportion to the duration of the affection. Tansard and Fleig<sup>2</sup> believes that the enlarged prostate can be reduced by exposure to the Röntgen rays. They recommend this treatment in cases which have not yet reached the stage of retention, for young patients, and for patients with an infected bladder, diseased kidneys, or of advanced years.

Such reports prove the enthusiasm of the reporter rather than the value of the method.

**ADRENALIN TO FACILITATE CATHETERIZATION.** Prince<sup>3</sup> relates three instances in which he and others had failed to introduce a catheter through a hypertrophied prostate; but after instillation of adrenalin and cocaine into the prostatic urethra the catheter was passed without difficulty. His method of applying the solution to the prostatic portion of the urethra is worthy of imitation. A solution is prepared by adding a small quantity of a 0.1 per cent. solution of adrenalin to an equal amount of 4 per cent. cocaine solution. An ordinary pipette is filled with this solution and inserted into the catheter. The fluid is allowed to gravitate to the tip of the catheter and the pipette is inserted into the upper end of the catheter, closing it and thus preventing the solution from escaping. The catheter is then introduced as far as possible without causing discomfort and the fluid injected from the catheter by pressing on the bulb of the pipette. In a short time the catheter will pass into the bladder to the great relief of the patient.

**MEDIAN PERINEAL PROSTATECTOMY** seems to have become the operation of choice with many surgeons in this country. The slight lesion, good drainage, brevity of anesthesia, freedom from evil consequences in the shape of fistulæ and cicatricial contractions, have established it in favor as the safest and most satisfactory operation when it is practicable.

<sup>1</sup> Münchener med. Wochenschrift, Nr. 14, 1907.

<sup>2</sup> Annales d. mal. d. org. gen.-urin., No. 24, 1907.

<sup>3</sup> Journal of the American Medical Association, January 5, 1907.

Most surgeons report that in a large minority—perhaps one-third—of the cases met, enucleation is impracticable by this route, because the prostate is too large or too fibrous, or the perineum too deep; in these cases either the suprapubic incision or the dissection of the perineum ("perineal prostatectomy") is done.

That the simple median urethrotomy permits enucleation of the prostate in all cases is maintained by Cunningham,<sup>1</sup> who reports 24 cases operated by this method without mortality, though not without complications. That a very large prostate can be enucleated by this method is shown by the removal of one which weighed a little more than one-half pound. Several items noted by Cunningham are of especial interest. He emphasizes the importance of the patient's taking a fair amount of nourishment during the convalescent stage. Next in importance in the after-treatment is getting the patients out of bed as soon as possible, as they are especially subject to hypostatic pulmonary congestion. Unless their condition will not allow of it, these patients should be placed in a chair the day following the operation.

Owing to the danger of infecting the wound and the possibility of forcing a thrombus from the prostatic venous plexus into the general circulation, with a fatal result, the bowels should not be allowed to move for two or three days. For controlling the bowels during these first few days Cunningham recommends the administration of pil. opii, gr. j, night and morning. He especially cautions against the use of enemas for at least a month because of the danger of dislodging a clot. The bowels should be moved, if necessary, by means of internal medication.

In regard to the suitability of this operation he states that while he is personally familiar with both the suprapubic and perineal dissecting operations, there was not a single case in this series in which he felt that one of the other methods would have been better. Of 14 patients who possessed sexual power before the operation, 6 retained the power unchanged, 1 considered it improved, 2 have not been heard from, 2 have not tried, and in 3 the power was lost. Of the 10 patients who had no sexual power before operation, 1 stated that it had returned. Cunningham found that the glands which were congested enucleated far easier than those in which there was no congestion. For this reason he is of the opinion that it is best to operate immediately upon those cases in which the congestion has caused acute retention, rather than to establish drainage until the congestion has been reduced, as is usually the custom.

The series was not free from complications. Hemorrhage occurred in 3 cases, requiring packing of the prostatic capsule with gauze saturated in an adrenalin solution. The hemorrhage occurred in 1 case shortly after operation, in another three days later, and in the third case the bleeding occurred ten days after operation and without any known cause.

<sup>1</sup> Boston Medical and Surgical Journal, May 9 and 16, 1907.

The hemorrhage in this last case was very severe; subcutaneous saline injections were necessary every six hours for three days.

There was no mortality in the series. Cunningham attributes this to (1) study of the character of the obstruction and changes in the bladder by means of the cystoscope and the functional capacity of the kidneys by the phloridzin test; (2) very short anesthetization and rapid operation; (3) encouraging the patient to live as near his normal life as possible during his convalescence.

THE SUPRAPUBIC OPERATION, on the other hand, is alone performed by some surgeons, notably Freyer. He reports<sup>1</sup> 119 additional cases operated on in ten months ending in July, 1906. The patients varied in age from fifty to eighty-six years, averaging sixty-eight years; the prostatic tissue removed varied from  $\frac{1}{2}$  ounce to  $9\frac{1}{4}$  ounces; 110 cases were entirely successful; 9 patients died between three and thirty-nine days after operation, some of them from causes quite independent of the operation. There were 39 consecutive operations without a death.

Bowers<sup>2</sup> believes that the transvesical route has become sufficiently perfected to assure a cure providing it is done before inflammatory processes have reached the kidneys and arrested their functional activity. He condemns the use of the catheter in cases of enlarged prostate, unless it is hopeless to interfere surgically. Kümmel<sup>3</sup> is of the opinion that the dangers of the perineal and bladder routes are about equal. The choice of operation will depend on the following facts: If the prostate protrudes deep into the rectum and the belly wall is thick the perineal route is preferable, while if the prostate protrudes more into the bladder the transvesical route is to be preferred. The suprapubic method is, in Kümmel's opinion, simpler and easier to perform, besides taking less time to heal. There is, furthermore, less danger of incontinence and fistula formation. The use of the cystoscope will usually decide the operation of choice.

In spite of the brilliant results from the median perineal alone, and from the suprapubic alone, I am inclined to preserve the belief often expressed that neither is best suited to all cases, and that the operator should determine in advance—through bimanual and cystoscopic examination—which cases are not suitable for enucleation through the median perineal incision. My general plan is to make this incision and endeavor without extreme force to enucleate through it. Should such efforts fail, a suprapubic incision may be added, the perineal being used for drainage. It must be admitted that increasing experience decreases the number of cases that cannot be satisfactorily operated on through the simple perineal urethrotomy.

Kümmel states that age is not a contra-indication to prostatectomy.

<sup>1</sup> British Medical Journal, March 9, 1907.

<sup>2</sup> American Medicine, July, 1907.

<sup>3</sup> Archiv f. klin. Chirurgie, 1907.

Prostatectomy should not be performed, however, if there is advanced arteriosclerosis, chronic bronchitis, insufficiency of the kidneys which cannot be remedied, entire loss of contracting power of the bladder, or severe impairment of the general health. The only exception he would make is in the case of *cancer of the prostate*. Kümme! states that cancerous degeneration of the prostate is far commoner than generally supposed, and that removal of the diseased gland may be permanently successful.

A case reported by Littlewood<sup>1</sup> is of interest because of the extreme age of the patient. He removed a vesical calculus weighing 2½ ounces and a prostate weighing 3 ounces from a man ninety years of age. The patient recovered and died two years later from uremia.

PRIMARY SARCOMA OF THE PROSTATE is very rare. Powers<sup>2</sup> has recently observed a case. He was able to find but 19 cases recorded in the literature. Of this number 12 occurred in children under fifteen years of age; seven of the tumors were of the small, round-celled type.

Powers' patient was a man aged sixty, who had had no bladder symptoms two months prior to being seen. At this time he complained of some pain and discomfort on urination and he had to rise in the night to urinate. The symptoms rapidly increased in severity. He lost flesh and strength; complained of a constant pain in the hypogastric region and constant, though less severe pain in the rectoperineal region, and urination became increasingly difficult, painful, and occurred about every hour and a half. The urine was normal. Rectal examination revealed a very large, rounded, slightly nodular, balloon-like prostate. A provisional diagnosis of sarcoma was made. The operation was attended by alarming hemorrhage and great difficulty in removing the growth owing to its friability. Histologically the tumor proved to be a small, round-celled sarcoma. The patient died of a double pneumonia on the fifth day.

NITROUS OXIDE ANESTHESIA. The importance of avoiding ether and chloroform anesthesia in elderly patients cannot be exaggerated. The chief cause of mortality after any operation for prostatic hypertrophy—as well as in the cases not operated—is the addition of uremia to the sepsis already existing, urosepsis; the danger of this is notoriously enhanced by ether, and in less degree by chloroform. Nitrous oxide, according to our present knowledge, does not thus affect the kidneys; and by all who have employed it extensively is much preferred to the other anesthetics for operations upon prostate and bladder in elderly men. Considerable personal experience has convinced me that it is distinctly preferable, the only serious objection being the cumbersome apparatus required for its administration. Anesthesia by nitrous oxide may be prolonged indefinitely if air be admitted with the gas to the patient's lungs.

<sup>1</sup> British Medical Journal, November 7, 1906.

<sup>2</sup> Transactions of the American Surgical Association, 1907.

Bevan<sup>1</sup> has been using nitrous oxide for the past three or four years and is very favorably impressed with its value. He first began using it in cases where ether and chloroform were specially contra-indicated, as in operation on the kidneys, in nephrotomy for anuria, abscess, etc. He then extended its use to kidney-stone operations and nephrectomies. As the anesthesia can be maintained for a considerable time, Bevan now employs nitrous oxide in a large proportion of his surgical cases.

He mentions as disadvantages the cumbersomeness of the apparatus when operating in any place except a hospital, and the expense. For work in private houses several small cylinders of the gas may be used.

The anesthesia is not so profound as by other methods, and the occasional talking of the patient may be disconcerting to the operator until he becomes familiar with the method. The very dark color of the patient's face and the dark blood in the wound are other factors which the operator must get used to. Bevan states that these disadvantages are offset by the great safety of the anesthesia, the rapidity of its action, the comfort with which the patient takes it, freedom from nausea, and almost immediate recovery from the anesthesia. In addition, complications affecting the lungs, kidneys, and liver are very infrequent.

**The Testicles.** TUBERCULOSIS OF THE TESTICLE is the subject of an excellent article by Keyes,<sup>2</sup> who reviews 100 cases; in 53 of these cases there was involvement of both testicles.

*Predisposing Causes.* Keyes does not place much reliance on a history of family tuberculosis, because certain pseudotuberculous, chronic, gonorrheal inflammations of the epididymis closely resemble tuberculosis and often occur in persons with tuberculous antecedents. In 27 patients a history of family tuberculosis was admitted, while in 14 it was denied.

Keyes admits the possibility of primary tuberculosis of the testicle, but has never seen a case. He says that in some of his cases the lesion in the testicle was the only one of moment, yet in all of these cases a careful examination showed some congestion of the prostate or vesicles or both. This congestion he regards as being always due to tuberculosis, the lesion in the testicle being an index of general tuberculosis of the genital organs. In confirmation of this view is the fact that only one of these patients was alleged to have begotten children after the involvement of one testicle. An analysis of these cases showed that the married ones usually ceased to beget children a year or two before invasion of the first testicle.

*Age.* Of these cases tuberculosis was first observed between the ages of fifteen and thirty-four in 71 per cent.; the testicle was first attacked in 65 per cent. between these ages. Keyes states that the date of onset of the tuberculosis is more important than that of its localization in the

<sup>1</sup> Journal of the American Medical Association, July 20, 1907.

<sup>2</sup> Annals of Surgery, June, 1907

testis, because it is impossible to regard tuberculosis of the testicle as a separate and distinct lesion apart from tuberculosis elsewhere in the body. Fixing the date of the original attack is furthermore of importance, as the disease may relapse even after years of quiescence, flitting between bone and lung and urinary tract.

*Exciting Cause.* In most cases there was no antecedent lesion that could rationally be accused of provoking the tuberculous infection. The current doctrine that gonorrhea is the common provocative was not sustained by Keyes<sup>1</sup> cases (indeed, we commonly see a tuberculous epididymis in boys who cannot justly be suspected of any sexual experiences). Injury and the hyperemia incidental to adolescence seem to be the commonest exciting causes.

Howard<sup>2</sup> has contributed a paper which is of interest in this connection. He has recorded 9 cases of tuberculous epididymo-orchitis in *children* under twelve years of age. The oldest patient was ten years of age and the youngest six and one-half weeks old. During the period (ten years) in which these cases occurred there were 149 instances of a tuberculous testicle in patients over twelve years of age. The total admission of male patients during this period was 55,912. In only 2 of these cases was there any marked history of tuberculosis in the family.

Keyes noted abscess of the vas in 11 instances and hydrocele in 30. He states that cases coming to operation nearly always show hydrocele or adhesions in the tunica vaginalis, showing that it has been inflamed. Tuberculosis of the vas is so common that Keyes does not think the divided end should ever be buried without providing drainage from it.

*Onset.* The onset was acute in 34 cases and chronic in 34. The chronic lesion shows a slightly sensitive nodule in the epididymis, while an acute epididymo-orchitis is associated with intense congestion and edema, and there is, in addition, fever and pain. The acute cases frequently resemble acute gonorrheal epididymitis; in one instance the process was so violent as to simulate strangulation of the testicle. Keyes is of the opinion that in cases with an acute onset as well as chronic cases with an acute exacerbation the exciting cause is a mixed infection. Caseation and fistula may, however, occur without any mixed infection. Breaking down of a pure tuberculous focus is certainly an unusual occurrence in tuberculosis affecting other parts of the body.

Breaking down of the focus, whether acute or chronic, simple or tuberculous, was noted by Keyes in 76 of the 153 testicles, and probably occurred in a great many more. He calls attention to the fact that softening commonly occurs in the first year (53 out of 76) and was noted only once each in the third, fourth, and fifth years. From these observations it would seem that if the process remained chronic in the epididymis for a year or two it is not very likely to break down.

<sup>1</sup> Annals of Surgery, June, 1907.

<sup>2</sup> British Journal of Children's Diseases, May, 1907.

Keyes followed for more than a year 35 cases that did not suppurate and 34 that did (one duplicate). Of the suppurating cases, 18 were still active when last seen, 12 of them within three years, 2 four, 3 five, and 1 six years; 16 either burst or were incised, and after suppurating for a number of months were seemingly cured. That a patient with a chronic focus in the testicle is never entirely free from the danger of supuration is evident from 1 case cited by Keyes, in which this occurred fourteen years after apparent healing as the result of an attack of gonorrhea.

He is not inclined to believe that such a percentage (30) of cures following suppuration would be verified if the cases were more numerous. On the other hand, cases which did not suppurate were constantly smouldering or advancing, simple cases showing irregular activity as late as five, six, eight, and ten years after the onset. Apparent cures were observed at five, eight, nine, twelve, and sixteen years in only 14 per cent.

*Condition of the Opposite Testicle.* Keyes states that many patients will permit one testicle to be removed in the hope that the disease is limited to this one organ and may thus be entirely eradicated. Unfortunately this hope is utterly vain, for relapse upon the opposite side usually occurs. Keyes found that the relapse practically always occurred within four years; hence, if the opposite testicle escapes for five years it is not apt to become infected.

Seven cases showing no infection of the opposite testicle for from seven to twenty-seven years will in all probability remain free. Keyes believes that such cases represent from 10 to 20 per cent. of the total number.

The three conditions with which the tuberculous testicle is likely to be confused are *simple epididymitis*, *syphilis*, and *neoplasm*. Keyes gives the following differential points:

1. Aspiration of hydrocele or drainage of abscess in order that the lesions of testicle and epididymis may be accurately palpated.

2. A familiarity with the clinical aspect of tuberculosis of the testicle—the little, rounded nodules; the diffuse infiltration of the epididymis; the acute epididymo-orchitis; the frequency of hydrocele and abscess; the ever-present sensitiveness to pressure.

3. Tuberculous family history, upon which too much weight must not be placed, and tuberculous personal history, which is often an important aid in diagnosis.

4. Evidences of tuberculosis in the internal genital organs, as evinced by active tuberculous lesions, chronic tuberculous nodules, or a slight haze in the urine and some pus in the prostate (which may be expressed by massage).

5. The diagnosis can be absolutely clinched by discovery of the tubercle bacillus in the urine, in the pus massaged from the prostate, or in the contents of the hydrocele fluid or the abscess.

Before excision of the testis or even of the epididymis is undertaken,

mercury and iodine should be administered in full doses for at least two weeks; experienced surgeons have repeatedly excised the syphilitic organ under the mistaken belief that it was tuberculous.

Keyes summarizes his conclusions as follows:

1. Testicular tuberculosis is clinically never an isolated lesion. It is only one feature of a general genital tuberculosis, for—

2. Sterility is probably frequent at the time the first testis is involved.

3. There is evidence at this time of inflammation of the internal genitals.

4. Relapse in the opposite testicle occurs within a few years in 8 or 9 out of 10 cases, and

5. Such relapse is nowise postponed by early removal of the diseased testis.

6. Moreover, though suppuration seems often to result in permanent cure of the local process, and

7. Though a chronic focus several years old is likely never to suppurate, yet

8. In no case can one feel certain of a real cure unless the tuberculous epididymis has been removed.

9. The demoralizing effect of epididymectomy is not to be compared with that of castration, and

10. Slight tuberculosis of the testis may be depended upon to heal spontaneously after removal of the epididymis.

11. Hence epididymectomy is the radical operation of choice, unless there is hyperacute generalized epididymo-orchitis, or unless the testis is destroyed by suppuration.

12. This operation has a beneficial effect upon the general health and upon tuberculosis of the internal genitals.

13. It should, therefore, be performed early in the disease. This in spite of the fact that

14. Tuberculosis of the testis is often but an insignificant part of a generalized progressive tuberculosis, or

15. Is for many years the only active lesion of the disease.

16. If the patient is sterile, it would probably be wise to remove both epididymes, even though only one side is diseased.

*Extirpation of the Vas and Seminal Vesicle* in cases of genital tuberculosis is advocated by Baudet and Kendirdjy.<sup>1</sup> From a study of 47 cases, including 4 in Baudet's own experience, they found that the extirpation had been through the perineal route in 30, while Young's method had been used in 3, the inguinal method in 6, the sacral in 2, and the parasacral in 5. Inasmuch as the operation is a serious one, it should not be attempted if there is a coexisting cystitis or extensive lung lesions. Age, however, need not be considered. The youngest patient in this series was

<sup>1</sup> Revue de chirurgie, No. 11, 1907.



three and the oldest sixty-two years of age. They advocate extirpation when there is a fistula due to a tuberculous seminal vesicle; when there is rectal obstruction or urinary disturbances not due to cystitis; when the vesicles are much enlarged or continue to enlarge after the subsidence of the epididymitis, and when there are manifest lesions involving the vas deferens.

ORCHITIS complicating *typhoid fever* has been observed in 2 cases by Gwyn.<sup>1</sup> The first case is of interest because of the peculiar and confusing distribution of the pain. In this case the onset was marked by severe abdominal pain in the region of the appendix, marked distention, a rise in the temperature and pulse rate, and muscular rigidity. The clinical picture suggested perforation. There was no leukocytosis. In a short time the right testicle became enlarged; the pain and swelling subsided in four days.

In the second case the orchitis developed in the fifteenth week. The organ became enlarged to the size of a goose-egg, was extremely tender, with pain radiating to the groin, and the constitutional disturbance was marked. In a week the organ suppurated and the abscess broke through the scrotum. Gwyn is of the belief that in this case the testicle was directly infested with the bacillus typhosus.

The after history of 14 cases of orchitis complicating *parotitis* is given by Rebaudi (abstract). The cases occurred in an epidemic several years ago. Of these 14 cases, 13 now have an atrophy of the testicle involved. Six of the cases show an hypertrophy of the sound testicle, and these men have begotten children, while none of the others have done so. Even in these cases with unilateral involvement there is now an absence of spermatozoa in the semen. Cases with gonorrheal antecedents were excluded. Rebaudi draws attention to the fact that the orchitis may be the only manifestation in mumps. This has not infrequently been noted in epidemics. He also states that orchitis may occasionally be associated with *tonsillitis*, with a resulting atrophy of the involved organ.

TRAUMATIC INJURY OF THE TESTICLES. Claims for damages due to injury to the testicles have resulted in two conflicting judgments in France. In one instance the insurance company was exempted from paying a claim, while in the other the plaintiff was sustained in his claims. Balthazard<sup>2</sup> has reviewed the subject of compensation due to insured wage-earners in industrial accidents. From a study of the physiology of the testicle he concludes that the only traumatic lesions of the testicle which might incapacitate a workingman are those which entirely destroy internal secretion. This, of course, would be more serious in a young than in an old man. Balthazard fixes the amount of incapacity at 50 per cent. for youths under twenty; for men over fifty at 10 per cent., or zero.

<sup>1</sup> American Medicine, February, 1907.

<sup>2</sup> Annales d. mal. d. org. gen.-urin., 1907, No. 12.

In regard to the *internal secretion of the testicle and the ovary*, Llewellyn<sup>1</sup> claims that they both contain an ingredient or ingredients which are antagonistic to the secretion of the thyroid gland. During the reproductive period of life the secretions from the testicle or ovary are the main factors in neutralizing the thyroid secretion. He has had 2 cases of *exophthalmic goitre* successfully treated with ovarian substance; both relapsed, however, as soon as the treatment was stopped.

*Torsion of the testicle* has been observed by Rigby and Howard in 9 instances. It is their belief that the basis for this accident is a congenital abnormality. The exciting cause, however, is obscure, several cases occurring without any ascertainable reason and while the patient was in bed and asleep. The severity of the attack, which is always sudden, depends on the tightness of the twist. Vomiting is a frequent and early symptom. Atrophy of the testicle usually results.

**STERILITY.** Pusey<sup>2</sup> is not of the belief that the *x-rays* are an important factor in the production of sterility. He states that in his experience this untoward effect of the rays has been greatly exaggerated. He cites the records of 7 women who had had numerous exposures, several as many as one hundred. Although no special care was taken, as it was before this possibility was recognized, none of the women were made sterile; all of them bore children within eighteen months after stopping the *x-rays*. Pusey states that he has no desire to belittle the untoward effects of the *x-rays*, but it is his conviction that the thing to be feared is a burn. If the rays are used within the limits of safety so far as burns are concerned, the other dangers can be practically disregarded.

Quinby<sup>3</sup> emphasizes the importance of examining both husband and wife in cases of sterility. When the male is at fault the trouble is not infrequently due to stenosis of the *vas deferens*, following an *epididymitis*. That this condition can be successfully met by an anastomosis between the *vas* and epididymis below the occlusion has been demonstrated by Quinby on guinea-pigs, and on dogs and men by Martin. A thorough knowledge of the anatomy of the parts is, of course, essential. After experimenting with suture material Quinby got the best results by using the finest sewing silk, No. 000, and dividing it into thirds. The silk was threaded into a so-called Bader's needle. He also found that the anastomosis could be more easily performed by splitting the *vas* longitudinally than after cross-section.

There are now on record a number of cases in which this operation has been successfully applied on the human subject. Martin's first case became the father of a child a year after operation, and in several others the presence of spermatozoa was demonstrated in the semen.

From an examination of male cadavers, Frank<sup>4</sup> found evidences of old

<sup>1</sup> Australian Medical Gazette, May 20, 1907.

<sup>2</sup> Journal of the American Medical Association, December 8, 1906.

<sup>3</sup> Boston Medical and Surgical Journal, November 8, 1906.

<sup>4</sup> Berlin. klin. Wochenschrift, 1907, Nr. 17

*inflammatory conditions in the vas deferens* in from 25 to 30 per cent. He furthermore states that statistics proved that *azoöspemia* is far more common than is usually thought, and that the most frequent cause of this is obstruction in the vas deferens. In order to prevent this trouble, he treats acute inflammation of the epididymis by means of heat. For this purpose he uses a flexible electric thermophore, which fits over the suspensory; starting with 40° C. the heat is gradually increased up to the tolerance of the patient. In addition, he prescribes a course of brine baths, as hot as can be borne.

Madden<sup>1</sup> calls attention to a group of cases with symptoms resembling those produced by a strangulated hernia, but which on operative interference proved to be cases of *cellulitis of the spermatic cord*. Two of the cases gave a history of having suffered for many years from hernia.

Whitney<sup>2</sup> gives the following interesting facts concerning *spermatoceles*. A spermatocele is practically a retention cyst and originates as the result of some external or internal affection of the seminal tubules. Clinically it presents itself as an enlargement of considerable size. The contents of the cyst consist of a non-albuminous fluid with a great number of spermatozoa. The condition is rare and its nature is not readily recognized before tapping. The position of the testicle is of aid in the diagnosis. Satisfactory results are obtained either by the injection of irritating solutions or by an operation.

Barberio<sup>3</sup> has devised a test for the recognition of *spermatic fluid*. The method is of some importance from a medicolegal standpoint, as the only known test available is the microscopic examination for the presence of spermatozoa; this fails in cases of *azoöspemia*. The test consists in the addition of a concentrated aqueous solution of picric acid to spermatic fluid, which causes a deposit of yellowish, rhombic crystals. A drop of saturated aqueous or alcoholic solution of picric acid is added to the suspected substance on an object glass and carefully heated until nearly dry, then another drop is added, and so on, thus producing a concentrated solution. Levinson<sup>4</sup> has tested the method and demonstrated that the reaction is not due to spermatozoa, as it was obtained in known cases of *azoöspemia*.

**Hermaphroditism.** An interesting instance of this anomaly is reported by Webster.<sup>5</sup> The patient was a man, aged thirty-three, who was admitted to the hospital with symptoms of acute peritonitis. Inasmuch as he had had an irreducible scrotal hernia for years, it was believed that the symptoms were due to strangulation. At the operation no hernia was found but instead a structure which looked like an adult uterus with tubes and ovaries. The mass, which was adherent around the inguinal

<sup>1</sup> Lancet, February 23, 1907.

<sup>2</sup> American Journal of Urology, May, 1907.

<sup>3</sup> Berlin. klin. Wochenschrift, 1906, Nr. 41.

<sup>4</sup> Ibid.

<sup>5</sup> Surgery, Gynecology, and Obstetrics, April, 1907.

ring, was removed. The patient, who was practically moribund, died shortly after operation. Examination of the specimen by careful dissection and microscopic study showed it to consist of a uterus and tubes. What seemed to be the ovaries proved to be the testicles. They occupied the same position with relation to the uterus that the ovaries do, but were of a complex structure. The tubes had the characteristics of those of an adult female, except the fimbriae were not so complex, being fewer in number. On one side there was more marked ovarian or testicular fimbriation. Examination of the broad ligaments showed a cyst on one side. Both round ligaments were present, the one on the side containing the cyst being flattened out and thin. Careful examination of the broad ligaments demonstrated a slightly convoluted tube, about 4 mm. in diameter, extending from the upper inner portion of the broad ligament toward the cervix. The tube was firm and had the consistence of a pipe-stem. Webster was able to demonstrate the Wolffian duct and vas deferens, also the cervix and prostate. This man was the father of twin children.

**Priapism.** Terrier and Dujarier<sup>1</sup> have observed a case of idiopathic persistent priapism. A study of 38 cases recorded in the literature showed that the priapism was associated with *leukemia* in 20 instances; in 2 it seemed to be due to a traumatic injury to the perineum and in 20 no cause could be discovered; 10 of the cases were submitted to operation; in 3 of them good results were obtained by incision of one or both corpora cavernosa. The condition of the part, however, seems to favor infection. In 2 cases the colon bacillus was found in the blood at the time of the incision. In the case observed by Terrier and Dujarier suppuration occurred in the right corpus cavernosum. It healed readily and there was no recurrence of the priapism.

Hobbs<sup>2</sup> has seen 3 cases of priapism due to *nasal irritation*, and he refers to 4 more reported by other observers. The details of Hobbs' last case are as follows: An unmarried man of thirty-three suffered much pain and discomfort from a nasal stenosis. On one occasion the pain had been particularly severe, due to increasing pressure in the nose. He was awakened the following morning with much pain in the head and face and intense pain due to a priapism. The priapism continued for three days, with only temporary remissions when he was completely under the influence of an opiate. Heat, cold, chloroform, etc., had no effect in reducing the priapism. A nasal examination at this time showed complete occlusion with outward bulging of the turgescient nasal tissues. To overcome this condition he was given 20 drops of adrenalin by mouth, and small pellets of cotton soaked in a strong solution of adrenalin and cocaine were gently insinuated; the cotton pellets were gradually

<sup>1</sup> Revue de chirurgie, vol. xxvii, No. 5.

<sup>2</sup> St. Louis Medical Review, September, 1, 1906

increased in size until finally a probe could be inserted. The nasal cavities were then sprayed with a weaker solution of adrenalin and cocaine. In about thirty minutes the patient experienced great relief from the nasal symptoms and at the same time the pain disappeared in the penis and that organ became less tense. The patient slept for about six hours, when there was some return of the symptoms; relief was given by repeating the treatment. For several months the nasal condition was treated locally with weak solutions of organic silver and adrenalin. This treatment, with some galvanocautery punctures to reduce the hypertrophies in the lower turbinates, effected a cure. A year and one-half later there had been no return of either the priapism or the nasal trouble.

Hobbs also mentions several patients coming under his observation in whom an erotic thought or sexual excitement produced sneezing due to nasal irritation. He attributes this to the close histological similarity existing between the turbinal tissues and the corpora cavernosa.

Turgescence of the turbinated bodies is a physiological accompaniment of turgescence of the sexual organs, especially in the female. It is well known that many female operatic singers refuse to sing during the first days of their menstrual periods, because of the nasal timbre of their voices during that time, due to nasal stenosis. Many women are conscious of swelling in the nose, with especially acute olfactory perceptions at the beginning of menstruation, as well as during sexual excitement at other times.

The cause for this turgescence—which involves all the erectile tissues of the body—is doubtless the retention of carbon dioxide and water, which regularly occurs prior to the menstrual period, and may occur in either sex at any time from imperfect excretion.<sup>1</sup>

It may well be doubted whether the swollen turbinates caused the priapism in Hobbs' cases; both were rather the result of a common cause, insufficient excretion; yet the coincidence is noteworthy.

**Urethral Irritation from Oxaluria** is believed by Swinburne<sup>2</sup> to be of not uncommon occurrence. He has observed 26 cases showing much the same symptomatology. There is a history of an attack of gonorrhea of recent or remote date. After the apparent cure of the gonorrhea there is persistence of a burning pain in the urethra, usually at the end of urination and sometimes quite sharp in character. There may or may not be a mucopurulent discharge. Examination of the urine shows, as a rule, nothing but a few shreds. Many of them are assured that the trouble is imaginary. Swinburne asserts that the true cause of these symptoms is oxaluria. Some cases readily yield to treatment, while in others the condition is stubborn.

<sup>1</sup> See The Weight Wave of Menstruation (Belfield), Journal of the American Medical Association, June, 1903.

<sup>2</sup> Journal of Urology, October, 1906.

**Gonorrhea.** THE PREVALENCE OF GONORRHEA. The present tendency to sensational exaggeration of the frequency of the remote evils of gonorrhea was depreciated in this review a year ago<sup>1</sup> in these words: "While it is doubtless wiser for physicians to exaggerate than to minimize the remote evils of gonorrhea in both sexes, yet there can be no doubt that the current tendency is to be sensational rather than accurate in dealing with this question." Further evidence supporting this conclusion is furnished by Erb,<sup>2</sup> who has been collecting data on this subject for some time. Several writers, who have been widely quoted, have asserted that the percentage of males who have acquired gonorrhea is over 80, and recently Blaschko has published a paper purporting to show that every man who did not marry until the age of thirty had had gonorrhea twice.

Erb takes a much more sane view of the question. He concluded that about 49 per cent. of 2000 men investigated had gonorrhea before marriage and that most of them contracted it before the age of twenty-five. He is also of the opinion that fully 45 per cent. of men entirely recover so that no traces of the disease are left. This is certainly a more optimistic view than that held by some genito-urinary surgeons. In 400 cases in which he had positive data he showed the effects on the wife from gonorrhea in the husband. Of these 400 women, 94 per cent. were free from any pelvic affection that could be ascribed to gonorrhea. In 68 per cent. of these families there were two or three children, and in 25 per cent. four or more, while in 44 cases there was only one child. The proportion of sterile marriages was less than 12 per cent.

GONORRHEAL PERITONITIS of the acute diffuse form occurring in the female is reviewed by Buford in connection with a case personally observed. He maintains that the abdomen should be immediately opened, and the infected organs, tubes, and even the uterus, removed; 6 cases in which this plan was followed have recovered. Thomas<sup>3</sup> reports 2 cases of gonorrheal peritonitis occurring in the *male*. In 1 case the infection was believed to have come from the seminal vesicles. The second patient denied ever having had gonorrhea.

EFFECTS OF GONORRHEA ON INFANTS. In a study of 250 breast-fed infants during the first ten days of life, Lobenstine and Harrar<sup>4</sup> were able to demonstrate the presence of the gonococcus in the genital tract of 50 of the mothers. Their conclusions are as follows: (1) The average birth weight of babies of gonorrheal mothers is less than that of babies of normal mothers. (2) The average initial loss is more pronounced in the gonorrheal babies (5.82 per cent., as against 4.74 per cent.). (3) The amount of loss regained on the tenth day is only 10.9 per cent. in the

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906, p. 139.

<sup>2</sup> Münchener med. Wochenschrift, 1907, Nr. 48.

<sup>3</sup> Northwest Medicine, March, 1907.

<sup>4</sup> Bulletin of Lying-in Hospital, December, 1906.

gonorrheal babies, as against 49.3 per cent. in the normal babies. (4) The gonorrheal babies show both more temperature disturbance and more intestinal disturbance than normal babies. (5) The babies of non-gonorrheal febrile mothers show a greater average initial loss than the normal babies, and regain at the time of discharge but 5.3 per cent. of their loss, as against 49 per cent. in normal babies.

**TREATMENT OF GONORRHEA.** The *serum treatment* of gonorrhea has been undertaken and its results reported by several observers, following the initiative of Torrey and Rogers.<sup>1</sup>

Swinburne<sup>2</sup> used it in 13 cases of acute gonorrheal epididymitis, and as a result states: "My impression of these cases is that the serum exerted a distinct effect in all the cases, and that the course of the disease was distinctly modified by it to a marked degree. The duration of the disease was distinctly shortened and in several of the cases the quickness of recovery was remarkable."

Swinburne observed no especial effect upon the urethral infection.

Hollister<sup>3</sup> states that so far as can be judged from a study of about 20 persons the *opsonic index* in gonococcus infections is usually low, but can be invariably raised and maintained at a higher level. His impression is that *vaccine therapy* is particularly promising in these conditions. Cole and Meakins<sup>4</sup> have treated 15 cases of *gonorrheal arthritis* by means of vaccines with results which, on the whole, were favorable.

**TREATMENT OF GONORRHEAL EPIDIDYMITIS BY MAGNESIUM SULPHATE SOLUTION.** This therapeutic application is described by Tucker.<sup>5</sup> The method employed is as follows: The patients are confined to bed and the bowels thoroughly evacuated. The scrotum is elevated by a towel twelve inches wide rolled up until about two inches in thickness. This is placed beneath the scrotum and held in place by tapes on either side, fastened in front and behind to a band encircling the body. A T-bandage will answer the same purpose, the tail being divided and one end being brought up on either side of the scrotum. The entire scrotum is covered with about fifteen to twenty thicknesses of gauze, which is saturated with a saturated solution of magnesium sulphate, the gauze being kept moist without changing, to avoid unnecessary handling of the part. With this treatment the pain is relieved in from three to twelve hours, and the swollen epididymis reduced to almost normal in a few days.

Uhle states that this has become the routine method of treating gonorrheal epididymitis at the Philadelphia General Hospital.

From considerable personal experience I can recommend this procedure.

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906.

<sup>2</sup> Transactions of the American Association of Genito-urinary Surgeons, 1906.

<sup>3</sup> Illinois Medical Journal, July, 1907.

<sup>4</sup> Johns Hopkins Hospital Bulletin, June and July, 1907.

<sup>5</sup> Therapeutic Gazette, April 15, 1907.

**Pus Tubes in the Male and their Treatment.** In *PROGRESSIVE MEDICINE* for December, 1905, p. 137, I called attention to the value of direct medication in vesicle infections. The importance of these infections and the simplicity of the method of treatment is, I think, sufficient excuse for again bringing up the subject. The following extracts are from a paper recently published:<sup>1</sup>

Pus infection of the seminal tube, including the vesicle, appears to be quite as frequent as pus infection of the Fallopian tube in the female. It is, however, not so often recognized, for its usual symptoms—pyuria, frequent and painful urination, and partial or complete retention of urine—are usually referred to the bladder and prostate, and the patient therefore treated for cystitis and prostatitis.

The infections of the seminal tubes are three—the gonococcus, pyogenic bacteria, and the tubercle bacillus; as the last induces suppuration only with the aid of the pyogenic bacteria, it will be omitted from consideration as a cause of pus tubes in the male. The pus infections of the seminal tube are extensions from the deep urethra; they result from (1) gonorrhea, (2) stricture, (3) prostatic concretions, and other causes of prostatic suppuration in middle-aged and elderly men.

Invasion of the seminal vesicle by the gonococcus induces the symptom complex usually considered indicative of prostatic abscess—frequent and painful urination, complete retention of urine terminated by a sudden discharge of pus, often an ounce or two, into the urethra. These phenomena are usually due to abscess formation in the seminal vesicles, as emphasized by Lloyd fifteen years ago; or in the utricle, as shown by myself twelve years ago.

Stricture of the bulbous urethra favors pus infection, which, beginning in the poorly nourished tissues, extends backward through the deep urethra into the seminal duct and vesicle, at times even to the epididymis. As the infection may extend forward in the urethra also, and thus produce a pus discharge from the meatus, the entire clinical picture simulates a gonorrhea, and by physicians who neglect to examine the pus with the microscope it is often so called—to the disgust and indignation of the innocent patient.

The non-gonorrheal infections of the seminal tube in men over forty years of age are, like everything else causing bladder symptoms in these patients labelled “prostatic hypertrophy;” and they do indeed cause the same symptoms, including even complete retention of urine. These are the cases of alleged prostatic enlargement that were benefited by vasectomy when that operation was popular. The prevalent rage for prostatectomy causes the unfortunate subject of vesiculitis to be accused of harboring an enlarged prostate and to be condemned to prostatectomy.

The pus infections (non-gonorrheal) of the seminal tube, especially

<sup>1</sup> New York Medical Record, May 4, 1907.



in elderly men, constitute an almost wholly neglected field; the obvious explanation is that already indicated—namely, the practical identity of symptoms with those caused by infections of the prostate and bladder, from which pus tubes have not been clinically distinguished. One whose attention has never been directed to this topic will be surprised to discover the number of cases treated for cystitis, prostatitis, and “prostatic enlargement” whose lesions are really pus infections of the seminal tube and vesicle. The differential diagnosis is by no means difficult; the usual mistake in diagnosis arises from the habitual failure to recognize pus tubes as the cause of pyuria, frequent and painful urination, and partial or complete retention of urine.

Fuller,<sup>1</sup> whose studies on the pathology and treatment of seminal vesicle disease are most favorably known, also emphasizes the dependence of bladder symptoms upon vesicular disease. He narrates a series of cases in which the classical symptoms of *cystitis*—frequent and painful urination and pyuria—were relieved by incision and drainage of the seminal vesicles. Fuller states that in his earlier cases *seminal vesiculotomy* was performed for the relief of the usual symptoms, chiefly of a sexual nature, which accompany chronic inflammatory involvement of the seminal vesicles. A study of the results obtained in these cases showed that the coexisting cystitis spontaneously disappeared after convalescence from the operation. He then undertook a cystoscopic study of the bladder in cases of seminal vesiculitis. As a result of this investigation Fuller found that in those cases where the bladder was involved the lesion was confined to the base of that organ, in fact, to that part of the structure lying over the seminal vesicles. Furthermore, in cases where the inflammation about the seminal vesicles was extensive the inflammation invading the base of the bladder was extensive and had extended farther than the underlying limits of the seminal vesicles. In all these cases the other portions of the bladder wall were normal or nearly so in appearance.

In mild cases the cystoscope showed the vesical mucous membrane of the area involved, red, infiltrated and edematous, while in the severe types granulation tissue had in large measure taken the place of the mucous surface. Here and there on these granulations were pus flocculi, films of inflammatory exudates, and spots of hemorrhage. A fairly free hemorrhage could be induced by instrumental contact in some of the advanced cases.

Fuller classes these bladder inflammations as localized pericystitis. He thinks it is reasonable to infer that the lesions of the vesical bases accounting for the cystitis were really peripheral ones, the centre foci for which were the infected seminal vesicles, the germs in the bladders having penetrated the intervening tissues from the cavities of the seminal

<sup>1</sup> Journal of Urology, December, 1906.

vesicles. Since these investigations Fuller states that he has performed seminal vesiculotomy for the express purpose of relieving these bladder conditions. So far he has had no failures.

**GONORRHEAL VESICULITIS.** Brunner<sup>1</sup> maintains that this condition is not infrequent. In order to secure the contents of the vesicle uncontaminated by other secretions he has the patient pass an ounce or two of urine; the prostate is then massaged, the patient again urinates, and the urethra is rinsed out with a solution of boric acid. The bladder is then filled with a boric acid solution, the catheter withdrawn, and the seminal vesicle on the side of the epididymitis is manipulated with the fingers. The contents of the bladder are then withdrawn and centrifugated. The sediment is stained with methylene blue and examined for gonococci and leukocytes. In doubtful cases the Gram method is employed. Brunner had positive findings in 16 out of 20 cases of gonorrheal epididymitis. In other cases leukocytes alone were found; in only 1 case were the findings negative. The seminal vesicle was swollen in 15 of the cases in which this "complete expression method" was employed. He advises the application of this technique in every case of gonorrheal epididymitis. The cleansing of the urethra and massage of the prostate, he thinks, removes the danger of error from admixture of secretion from other parts.

<sup>1</sup> Journal of the American Medical Association, March 9, 1907.

# PRACTICAL THERAPEUTIC REFERENDUM.

By H. R. M. LANDIS, M.D.

IN reviewing the articles dealing with treatment which annually appear, one cannot but be impressed with the fact that each year there is an increasing number of contributions devoted to the hygienic management of disease. The use of rest or the regulation of exercise, attention to ventilation and fresh air, and the prescribing of a suitable dietary are matters of the utmost importance whether the particular disease be acute or chronic and whether drugs be employed or not.

The diseases for which there is a specific drug are unfortunately few, but even in these the results can be greatly improved if attention is paid to the general hygienic requirements of the patient. In *PROGRESSIVE MEDICINE* for December, 1906, a series of articles dealing with the treatment of syphilis was reviewed. The opinion expressed by the writers of these articles was that instructions as to bathing, diet, exercise, hours of sleep, and fresh air were almost as important as the administration of mercury; indeed, one of the writers went so far as to say that many individuals suffering from syphilis would recover without mercury if these principles were followed.

If a very considerable space has been given in the present review to therapeutic measures other than drugs, it has been because a knowledge of these measures is necessary if the highest degree of success is to be attained.

It should not be understood that the use of drugs has depreciated or that we will ever arrive at a time when they will not, as now, play a most important part in the treatment of disease. The important fact to keep in mind is that common sense should dictate the use of drugs and remedial agents other than drugs, and that indiscriminate prescribing is to be as much deplored as therapeutic nihilism.

"Finally," to quote from a recent editorial article on "Therapeutics and Common Sense,"<sup>1</sup> "let us recollect, whenever we are tempted to administer remedies too freely, that, after all, drugs and remedial measures other than drugs are designed to help nature, not to force it; that in many instances nature, if left to itself, will produce cures which are so far beyond our comprehension as to be perfectly marvellous; and let us inculcate into the minds of our students and patients the fact that quiet and rest and patient waiting for nature's processes will often pro-

<sup>1</sup> *Therapeutic Gazette*, September, 1907, p 627

duce a cure most quickly, particularly if gentle remedial measures are cautiously employed.

"Let us give drugs bravely and fully when there is good reason for their administration, and refuse to give drugs, with equal bravery, when a careful examination of the patient convinces us that he will do best without them."

**Adrenalin.**—During the past three years a great deal of experimental work has been done with adrenalin. The most notable discovery in this connection seemed to be that the injection of adrenalin into rabbits was capable of producing lesions in the aorta similar to human aortic atheroma. This fact was important for two reasons: first, it raised the question as to whether large doses of adrenalin could be safely used without leading to arterial changes, and, second, it gave the opportunity of producing experimental lesions in animals which would tend to throw light on the early changes in arteriosclerosis. During the past year two interesting reports have appeared on this question, both of which seem to show that the deductions drawn from the earlier work are open to criticism.

Kaiserling,<sup>1</sup> in repeating these experiments according to the recognized technique, obtained negative results in a series of eight rabbits, although in one case forty-four injections, amounting to 19.3 c.c. of adrenalin hydrochloride, were given in a space of ninety-four days. These results, together with the fact that he accidentally discovered calcification of the aorta in a rabbit untreated, have rendered Kaiserling very skeptical of the relationship between adrenalin and atheroma. He suggests that diet, age, and breed may be factors in the production of the atheromatous changes and that before the question can be definitely settled many more animals must be studied.

Still more striking results have been recently obtained by Miles and Johnstone.<sup>2</sup> These observers found that of sixty-one rabbits that had received adrenalin, but seventeen, or 28 per cent., showed arteriosclerosis, whereas of fifty-eight supposedly normal rabbits similar lesions were found in twenty, or 34.5 per cent. Miles, in a study of the literature on adrenalin arteriosclerosis, found that as a rule the experiments had not been adequately controlled.

Carleton<sup>3</sup> advocates the external use of adrenalin for the relief of *neuralgia*, *neuritis*, and *reflex* or *referred pain*. The article contains the opinion of a number of observers who have had success with the treatment.

The drug is used in the form of a 1 to 1000 ointment, which is thoroughly rubbed over the distribution of the offending nerve. The amount to be used in any affection of a peripheral nerve should not exceed 1 to 2

<sup>1</sup> Berliner klin. Wochenschrift, December 31, January 14, 1907.

<sup>2</sup> Journal of the American Medical Association, October 5, 1907.

<sup>3</sup> Therapeutic Gazette, May, 1907; American Medicine, February 24, 1906.

minims, except in the case of the sciatic nerve, when 2 to 3 minims may be used. Larger quantities often produce ischemia, which might prove injurious in some cases, notably when application on or near the spine is necessary.

The usual time for relief is three minutes. Carleton states that the treatment is apt to fail without a knowledge of the distribution and functions of the nerves and ganglia. For information on this subject he recommends Toldt's *Anatomy*, part vi, and the tables of the nerves and of the ganglia in Gould's *Dictionary*. The treatment seems to have been especially useful in those instances of nerve pain of which *sciatica* is an example. For the treatment of *sciatica* 2 or 3 minims of the ointment should be applied over the course of the nerve from where it comes from under the gluteal fold, and for about three inches down, and about as much from the sciatic notch upward. Potts<sup>1</sup> reports two cases of *sciatica* that were relieved by the adrenalin ointment and in which there was no recurrence.

Ferguson<sup>2</sup> recommends adrenalin in the treatment of *rattle-snake bites*. His treatment consists of adrenalin chloride hypodermically in sufficient doses and often enough to strengthen and sustain the heart until the poison is eliminated; opium in some form for the pain and the incising and injecting of the fang wounds with a strong solution of *permanganate of potassium*. The use of adrenalin in association with permanganate of potassium and the use of permanganate alone has been previously mentioned.<sup>3</sup> It is probably true of this report, as of other similar ones, that the beneficial effects were due to the permanganate of potassium rather than the adrenalin. The report of last year on the use of the permanganate alone was especially convincing as to the value of this method of treating snake bites.

**Alcohol.**—For the past three years the attempt has been made in these pages to present the prevailing views on the use of alcohol. Every year writers have presented the most divergent opinions based either on experimental or clinical observations to show that alcohol is or is not a food; that it is a valuable stimulant or that it is utterly useless as such; that it increases the bactericidal properties of the blood or that it renders the organism more susceptible to infection. The past year has seen an even larger literature on alcohol than for some time. Alcohol formed the subject of a symposium at the Montreal meeting of the British Medical Association in 1906, and also during the past year the *Journal of the American Medical Association* has published a series of articles dealing with the alcohol question in its various phases. Besides, numerous articles have appeared in both the foreign and American journals. An editorial<sup>4</sup> comment on the discussion before the British Medical Asso-

<sup>1</sup> Loc. cit.

<sup>2</sup> Texas Medical Journal, November, 1906.

<sup>3</sup> PROGRESSIVE MEDICINE, December, 1905, p. 286; December, 1906, p. 326.

<sup>4</sup> Journal of the American Medical Association, October 6, 1906.

ciation is very apt: "The discussion has not increased our knowledge on the subject to any appreciable degree. To all intents and purposes, so far as the elucidation of moot features of the alcohol question is concerned, we are where we were."

It would be idle to deny that the excessive use of alcohol is to be deplored. Undoubtedly some of the evils to which the human race is heir are brought about by alcohol. This is particularly true of certain affections of the nervous system such as idiocy and epilepsy. Mental defects and other forms of degeneracy are far more frequent in the children of alcoholics than in non-alcoholics or in those using the drug temperately. That alcohol plays any part in the causation of consumption, except through the production of poverty, is questionable. Granting all this, there is no need, as some apparently wish, of confusing the legitimate medical uses of alcohol with the sociological evils arising from its excessive use. We have yet to learn that it would be a wise thing to banish opium from the *Pharmacopœia* because of the frequency of the opium habit.

The *Therapeutic Gazette*,<sup>1</sup> in an editorial criticism of certain claims against alcohol, puts the question, I think, very clearly: "If the ethical and economical questions concerning the employment of alcohol as a beverage were entirely divorced from the therapeutic question of its employment as a remedy, there would be less confusion in the minds of the laity and of the profession than exists at the present day. At times the ethical problems cross the lines of the therapeutic problems, and when this is the case it is the duty of the physician to remember that there are two sides to the matter. Personally, we are firmly convinced that in many diseased conditions alcohol is a most valuable drug. We do not belong to that class which considers that it acts as a stimulant in the ordinary sense of the term, in that it increases the activity of the heart, respiration, or of the nervous system, but we think that it is a stimulant in the sense that it supports vital processes in disease, although not in all cases of disease. The experience of the profession that it is a valuable adjunct to quinine and iron in combating septicemia in many cases has not, in our minds, been in the slightest degree controverted by the scientific investigations which have been carried out upon healthy animals and healthy men within the last few years."

**Antidiphtheritic Serum.**—The literature on this subject has been very extensive during the past year and, while nothing new has been advanced, many important points have been emphasized.

The subcutaneous method of administering the antitoxin is practically universally used and would be perfectly satisfactory were it not for the increased cost incurred in preparing the antitoxin so that it can be given by a hypodermic syringe. An additional objection is the danger of

<sup>1</sup> December, 1906.

infections following a hypodermic injection. This last objection, however, can be practically disregarded if ordinary antiseptic precautions are observed. McClintock and King<sup>1</sup> have published the result of original research work on the *oral* administration of antitoxin. They found that while the oral administration of antitoxin cannot be relied on to give the results obtained by hypodermic administration, the antitoxin is absorbed as such from the stomach. It was also found that diphtheria and tetanus antitoxin when mixed with trikresol, salol, chloroform, and opium were much more effective when given on an empty stomach. The result of this research would indicate that if for any reason antitoxin must be given by mouth it should be during a period of starvation, as the stomach juices act deleteriously upon the antitoxic substances. McClintock and King could not determine which substances were most suitable to diminish digestive activity. The substances named above, and which are commonly mixed with the antitoxin for preservative purposes, seemed to cause a more rapid absorption than when antitoxin alone was given.

Another method of administering antitoxin is *intravenously*. Bisson<sup>2</sup> reports on this method in 200 cases, all of a very severe type. Park<sup>3</sup> would reserve this method for very severe cases and never employ it in the ordinary types of the disease.

Diphtheria has been robbed of a large part of its terror through the knowledge that it can be prevented by the use of immunizing doses of the antitoxin. Outbreaks of diphtheria in institutions are no longer the fearful scourges they once were. The usual immunizing dose is 500 units; some, however, employ but 300 units, and others give as much as 1000. Shackelton<sup>4</sup> in an outbreak of diphtheria in a school used 2000 units. Terrible<sup>5</sup> reports on 2500 immunizing doses in a recent epidemic of diphtheria. He employed about 300 units, which conferred an immunity for nineteen to twenty days. Of 2000 cases so treated 17 developed the disease, but always in a mild form and none died. Brown<sup>6</sup> reports on an epidemic occurring in the Adirondack Cottage Sanitarium for the treatment of tuberculosis. He employed 500 units for immunizing purposes, but found that such doses had to be repeated every two weeks during the occurrence of the diphtheria.

Purdy<sup>7</sup> questions the efficiency of 500 units as an immunizing dose. He used this amount in a family in which one of the children died of malignant diphtheria. While diphtheria developed in the others, it was mild. I do not think that it can any longer be questioned that temporary immunization is possible. Even when given some time after expo-

<sup>1</sup> Journal of Infectious Diseases, October 30, 1906.

<sup>2</sup> Lancet, October 6, 1906.

<sup>3</sup> Medical Record, 1906, p. 478.

<sup>4</sup> Lancet, September 15, 1906.

<sup>5</sup> Gazzetta degli Ospedali, 1907, xxviii.

<sup>6</sup> American Journal of the Medical Sciences, February, 1907.

<sup>7</sup> Journal of the American Medical Association, June 29, 1907.

sure or in insufficient doses the attack is almost invariably mild. Where the exposure to infection has been slight, 500 units are sufficient; in institutions this dose had best be repeated every two weeks. To those constantly exposed the immunizing dose should be not less than 1000 units. In all instances where the initial case is of a malignant type such as Purdy reports, the immunizing dose to those who have been exposed should be not less than 2000 units.

The curative effects of diphtheria antitoxin are now practically universally acknowledged. There are two factors, however, which keep the mortality higher than it should be: (1) The tendency to temporize and withhold the antitoxin until the diagnosis is positive. Such a practice cannot be too strongly condemned. If there is the remotest suspicion that diphtheria may be present, give the antitoxin at once and confirm the diagnosis later. Given on the first day the mortality is less than 1 per cent. and it increases in direct proportion to the time the antitoxin is withheld. (2) The dose of antitoxin employed is frequently too small and not repeated sufficiently often. Aside from rashes and joint pains, antitoxin is harmless. There are now on record a large number of cases in which from 50,000 to 125,000 units have been given with no ill effects. In young children there is especially a tendency to give too small doses. As Crookshank<sup>1</sup> points out, the dose of antitoxin has no relation to the age of the patient. Indeed, so far as children are concerned the dose should be larger than for an adult, as they are less able to withstand the infection.

The following table, published by the Chicago Board of Health,<sup>2</sup> points out very strikingly the dangers of delay. The figures are made up from 8372 cases of bacterially verified diphtheria treated with antitoxin, from October 5, 1895, to December 31, 1906:

	INJECTION MADE ON					
	First day.	Second day.	Third day.	Fourth day.	Later.	Totals.
Number of cases treated . . .	624	2181	2926	1578	1063	8372
Number of deaths . . .	2	33	99	176	234	544
Percentage of deaths . . .	0.32	1.51	3.38	11.15	21.01	6.50 <sup>3</sup>

These results need no comment. The well-demonstrated fact that antitoxin is a harmless agent and that large quantities can be given without untoward results makes it apparent that in any given case the error should be made of giving too much rather than too little.

Park<sup>4</sup> states that he studied experimentally the effects of various doses. He found that patients that received but 1000 units at the first injection

<sup>1</sup> West London Medical Journal, April, 1907.

<sup>2</sup> Journal of the American Medical Association, August 17, 1907, p. 514.

<sup>3</sup> The average mortality percentage of all cases is 6.50.

<sup>4</sup> Medical Record, September 22, 1906.



did worse than did those who received 2000 units; the latter did not do quite as well as those getting 3000 units. When larger doses were given, however, Park was of the opinion that there was little difference produced between those getting 6000 units and those receiving 12,000 units. On this point, however, other observers are not in agreement.

Studdiford,<sup>1</sup> Kirley,<sup>2</sup> and Crookshank,<sup>3</sup> in writing on the dosage of antitoxin, advocate a large initial dose (5000 to 6000 units). A good working plan for the administration of antitoxin in the various types of diphtheria is that in use at the Philadelphia Municipal Hospital. Details of this were given two years ago, but they may be profitably repeated.<sup>4</sup>

Purely tonsillar exudate (single), 2500 units; purely tonsillar exudate (double), 5000 units; tonsillar exudate with involvement of pillars and uvula or pharynx, 7500 to 10,000 units; nasal and any other part involved, 7500 to 10,000 units; laryngeal 7500 to 10,000 units. If the exudate is rapidly separating, do not give a second dose; where a great amount of exudate remains, give a daily dose of from 5000 to 7500 units until the greater portion has disappeared. When patients are seen after the seventh day of the disease, give 2500 units only and do not repeat.

Rosenau and Anderson<sup>5</sup> have shown experimentally in animals the beneficial effects of antitoxin in modifying diphtheritic paralyses. After the paralysis has appeared, however, the antitoxin was of no benefit. The epidemic reported by Lawrason Brown<sup>6</sup> is of interest in that it occurred in an institution devoted to the treatment of *tuberculosis*. The following conclusions are of interest: (1) In institutions where the outdoor treatment is rigidly enforced the epidemic will probably be cut short. (2) In the presence of a diphtheria epidemic patients with pulmonary tuberculosis should be treated, as regards the diphtheria, as otherwise healthy individuals. (3) When the tuberculous contract diphtheria they should be moved out of doors as soon as possible. (4) Mild diphtheria seems to exert little or no harmful influence upon the pulmonary lesion in tuberculosis. (5) The antitoxin in small or large doses seems to have little or no effect upon the pulmonary tuberculosis. (6) Immunizing doses may be given to patients with fever. (7) Complications seem to occur after diphtheria no more often, possibly less, in the tuberculous than in the non-tuberculous.

Aside from the familiar rashes and joint pains which sometimes follow the use of antitoxin, untoward effects are very rare. The following untoward effects are, I believe, rather unusual:

Wilbur<sup>7</sup> reports the case of a woman who shortly after receiving an immunizing dose of 1000 units, developed a rapid, forcible, and inefficient

<sup>1</sup> Medical Record, September 22, 1906.

<sup>2</sup> Ibid.

<sup>3</sup> West London Medical Journal, April, 1907.

<sup>4</sup> PROGRESSIVE MEDICINE, December, 1905, p. 291.

<sup>5</sup> Transactions of the Association of American Physicians, 1907.

<sup>6</sup> Loc. cit.

<sup>7</sup> American Journal of the Medical Sciences, August, 1906.

cardiac action. The mucous membranes became edematous and it was only with great exertion of the will-power that she retained consciousness. The patient had a feeling of impending death. A somewhat similar occurrence is reported by Avery.<sup>1</sup> In this instance, also after an immunizing dose of 1000 units, the patient lost consciousness, had marked dyspnea, and a feeling of chilliness which developed into a rigor. Avery mentions several similar instances in the literature.

For some unexplainable reason the sudden occurrence of such untoward symptoms is very frequent after the injection of Maragliano's *antituberculous serum*. In these cases almost immediately the patient becomes cyanotic, dyspneic, and pulseless. Often a severe lumbar pain is complained of and occasionally there is nausea followed by vomiting. The patients have a feeling of impending death. The attack is very short and after it has passed off the patient is as well as ever, although in some instances the lumbar pain persists. It is one of the most terrifying experiences imaginable. I have seen this effect twice after using Maragliano's serum, and have knowledge of some five or six similar occurrences.

The State Department of Health of Pennsylvania, which last year established stations for the distribution of antitoxin in the outlying districts, reports<sup>2</sup> on the results for the first six months of 1907. In 1712 cases given antitoxin for curative purposes the mortality was 8 per cent. The mortality during a corresponding period in 1906 was 11 per cent. Indiana has recently adopted the same plan and is ready to furnish to the poor free antitoxin.

Diphtheria antitoxin has been considerably used in the treatment of *cerebrospinal meningitis*. The results, however, have been far from satisfactory, many claiming that it has no effect in bringing about a favorable result. Balduzzi<sup>3</sup> reports favorably on the use of diphtheria antitoxin in fifty-nine cases of meningitis. He used the antitoxin to stimulate the defensive reactions of the body. In fulminating cases no benefit was observed, as the organism was incapable of responding.

**Antidysentery Serum.**—The efficiency of this serum in the treatment of the bacillary forms of dysentery has been demonstrated by Vaillard and Dopter<sup>4</sup> and Skschivan and Stefansky.<sup>5</sup> The serum is obtained by immunizing horses and is entirely harmless to man. Vaillard and Dopter report on ninety-six cases with most favorable results. The amount injected ranged from 20 to 100 c.c.; the dose was repeated sometimes in twenty-four hours, and in very severe cases a third dose was given. The intestinal disturbances rapidly cleared up. They found the curative

<sup>1</sup> American Medicine, October, 1906.

<sup>2</sup> Journal of the American Medical Association, August 10, 1907, p. 503

<sup>3</sup> Gazzetta degli Ospedali, 1907, xxviii.

<sup>4</sup> Annales de l'Institut Pasteur, 1906, xx, No. 4.

<sup>5</sup> Berliner klin. Wochenschrift, February 11, 1907.

effects of the serum so prompt and certain that its prophylactic use did not seem necessary. Similar results were obtained by Skschiran and Stefansky in fifteen cases treated at Odessa. The effect of the serum was noted in two or three days. The stools diminished in number and there was a decrease in the pain and tenesmus.

**Antistreptococcus Serum** continues to be the subject of isolated case reports, some favorable and others unfavorable to its use. Zangemeister,<sup>1</sup> who has used the serum in obstetrical patients, is not impressed with its value in septic conditions. He concludes that to date the serum has not proved reliable for the production of either active or passive immunity. Most clinicians will probably concur in this opinion.

**Antitetanic Serum.** For the past five years the *Journal of the American Medical Association* has done a most laudable work in pointing out the dangers of tetanus following Fourth of July injuries. Full directions as to the preventive treatment of such wounds have been repeatedly emphasized. This year<sup>2</sup> in a special article the results of the past Fourth of July are given. The following table is most interesting:

CAUSES OF TETANUS CASES.

	Blank cartridge.	Giant cracker.	Cannon.	Firearms.	Powder, etc.	Total.
1903 . . . .	363	17	5	3	27	415
1904 . . . .	74	18	5	1	7	105
1905 . . . .	65	17	4	5	13	104
1906 . . . .	54	17	1	7	10	89
1907 . . . .	52	8	6	4	3	73

It will be noted that in 1903 there were reported from all parts of the country 415 cases of tetanus, while the last Fourth shows but 73. This cannot be attributed to a natural decrease in tetanus, as reports of tetanus from wounds not obtained in Fourth of July celebrations are more numerous. This reduction is largely due, I believe, to improved methods of treatment. It is furthermore pointed out that while there has been this marked decrease in Fourth of July tetanus the mortality from other causes has increased from 60 to 102. This would indicate that there has been little restriction in the sale of giant crackers and blank-cartridge pistols, and that much remains to be done. It is almost incredible that a people will lend themselves to so senseless a celebration as that which we annually go through. Our most recent "jolly celebration" of Independence Day was achieved at the cost of 164 killed and 4249 injured, many of these maimed for life.

The principal causes of Fourth of July injuries, particularly tetanus, are the giant cracker and the blank-cartridge pistols. Medical skill can prevent the occurrence of tetanus in all of these cases; it cannot prevent, however, the permanent damage resulting from severe mutilating wounds. To eliminate these Fourth of July injuries entirely the

<sup>1</sup> Münchener med. Wochenschrift, 1907, liv, Nr. 21.

<sup>2</sup> August 24, 1907.

municipal authorities must be aroused to the gravity of the situation. Stringent laws should be passed forbidding the sale of such articles and, in addition, the daily press should be enlisted to educate the people.

In view of the importance of the subject it may be well to call to mind the following facts regarding tetanus: Starting from the local wound the tetanus toxin enters the motor-nerve plates of the muscles and thence passes up the motor nerves to the motor ganglia in the cord. Some of the toxin is taken up by the blood current, where it is either destroyed or is again conveyed to the nerve structures. The toxin shows a strong tendency to enter into combination with the higher nerve ganglia, and, once such a combination is effected, any form of treatment is usually unavailing. The knowledge of this combination, however, has led to the brilliant results of prevention in which the object is to eradicate the infecting source at once or prevent its ascent of the nerves by injecting antitoxin into the nerve supply of the affected part. Intracranial and intraspinal injections of tetanus antitoxin have been made with this same object in view in cases in which tetanus has already developed, namely, to reach the higher nerve centres as rapidly as possible. Porter<sup>1</sup> has suggested that the higher centres can be as quickly and more easily reached by injecting the antitoxin into either the hypoglossal or the spinal accessory nerve.

Tetanus is of two types: the acute, which develops within nine days after an injury, and the chronic form, which occurs later. The great majority of cures reported have been in the latter form; but very few cases have recovered where the disease has developed shortly after an injury.

It should be a routine practice that all Fourth of July wounds and all penetrating wounds contaminated by street dirt, at any time of the year, should be subjected to the following treatment: The patient should be anesthetized in order that the wound may be freely opened and thoroughly curetted. The wound should be kept open and allowed to heal from the bottom. The tetanus bacillus, being an anaërobe, thrives especially in wounds with a small entrance, which quickly becomes sealed; 5 to 10 c.c. of antitoxin should be injected into the nerve supply of the affected part and, in addition, a subcutaneous injection of 5 c.c. should be given. The eliminative organs should be stimulated. The evidence at hand is practically conclusive that such measures will effectually prevent the occurrence of tetanus. Even if it is impossible to obtain antitoxin, thorough cleansing of the wound by curetting should be done.

In this country there has been no instance of tetanus antitoxin failing as a prophylactic. In European literature Suter<sup>2</sup> and Terrier and Mercade<sup>3</sup> have noted twenty-four cases in which failure occurred. An editorial comment<sup>4</sup> on these cases calls attention to the fact that in some

<sup>1</sup> Boston Medical and Surgical Journal, September, 6, 1906.

<sup>2</sup> Beitrage Zeit. klin. Chirurgie, 1907, p. 694. <sup>3</sup> Revue de chirurgie, 1907, No. 1.

<sup>4</sup> Journal of the American Medical Association, August 17, 1907.

of these cases the interval between the time of infection and the time of injection of the antitoxin had been too long; in a few there was reason to believe that the antitoxin was inactive and in a few antitoxin powder had been used. It is noteworthy, however, that of these twenty-four cases in which tetanus developed after the prophylactic dose of antitoxin, about two-thirds recovered. These facts emphasize the necessity of using the antitoxin at once in any wound in which there is a possibility of tetanus developing and in seeing that the serum used is of recent date.

Strock<sup>1</sup> advocates large doses of the antitoxin. His experience with tetanus had been characterized by failure (not a single case recovering) until he started using the antitoxin in frequent doses. He believes that at least 10 c.c. should be given every hour until evidences of improvement manifest themselves. Since employing the antitoxin in larger quantities three of the last five cases treated have recovered.

Kinyoun<sup>2</sup> has tried dried tetanus antitoxin in the treatment of wounds infected with tetanus, but with little or no success in preventing the disease in the case of deep or penetrating wounds. In minor superficial wounds, many of them contaminated with street dirt, the powdered antitoxin was given an extended trial. It was found that wounds so treated healed more rapidly and with less disturbance than wounds treated in the ordinary way. A number of infected wounds were treated in this way with equally good results. Kinyoun believes that the uniformly good results indicate that the dried serum possesses qualities other than its specific body, the antitoxin. He is of the opinion that this other quality is an immune body, which, when brought into contact with the tissues, becomes bactericidal. Experimentally Kinyoun has found that serum from an immunized animal is more bactericidal than normal serum.

**Antimeningitic Serum.** The extensive epidemic of cerebrospinal meningitis, numbering some 4000 cases, with a mortality of 75 per cent., which occurred in New York City two years ago, resulted in the appointment of a commission to study this disease. The experimental work of Flexner,<sup>3</sup> as a member of this commission, is most interesting and bids fair to lead to most important results. Cerebrospinal meningitis is undoubtedly due to the diplococcus of Weichselbaum. In monkeys Flexner was able to produce the disease as it is seen in man. The monkeys developed retraction of the head, nystagmus, a comatose condition, and other manifestations as seen in man. Pathologically the lesions did not occur in a haphazard way, but conformed to the distribution met with in the human being.

In this connection the principal interest lies in the results obtained with

<sup>1</sup> Medical Record, July 27, 1907.

<sup>2</sup> Ibid., October 20, 1906.

<sup>3</sup> Preliminary Report, Transactions of the Association of American Physicians, May, 1906; Journal of Experimental Medicine, March 14, 1907, vol. ix, No. 2; International Clinics, 1907, No. 2.

the production of a serum. In addition to Flexner's work in this line two other contributions have appeared, one by Kolle and Wassermann<sup>1</sup> and the other by Jochmann.<sup>2</sup> Serum was produced at first by immunizing a goat and large rabbits; later a horse was used. The serum from the latter animal was used in protecting monkeys experimentally inoculated. It was found that the simultaneous injection of the serum and of the culture of the diplococcus prevented the development of the disease. If the serum was injected into the spinal cord even six hours after the diplococcus, the monkey did not die. Flexner states that several animals were undoubtedly saved in this way. Large doses of serum given subcutaneously acted favorably in some cases, but all cases did not respond to this method. In spite of the encouraging results obtained in animals, Flexner takes a very conservative view. He states that so far as humans are concerned there is difficulty in estimating exactly the duration of the disease and the applying of the serum at the most favorable stage. Flexner used in the controls a mixture of the animal's normal serum with the injected culture. Even this normal serum was found to have, to some extent, a certain definite protective value. In commenting on this fact Flexner states that as normal serum exercises a certain degree of protection, advantage of this fact might be taken in cases of human infection. It would, of course, be practicable to obtain normal human serum for such injections. As he states, the gravity of the disease and the absence of any efficient therapeutic measure against cerebrospinal meningitis render this fact worthy of consideration.

**Apomorphine** is highly recommended by Rosenwasser<sup>3</sup> in the treatment of *acute alcoholism*. It is generally recognized that apomorphine given hypodermically is an excellent emetic. Rosenwasser states that in the eight years which have elapsed since Douglas pointed out that apomorphine was a valuable hypnotic, but little attention seems to have been paid to this action of the drug.

It must be remembered that when exposed to the air apomorphine rapidly decomposes and may give rise to dangerous symptoms. The solution should always be fresh and is preferably made from hypodermic tablets obtained from some reliable source. It occurs in two forms, the crystalline and the amorphous. The latter should never be employed, as it is capable of producing dangerous, even fatal effects.

The hydrochloride of apomorphine is the salt employed, the emetic dose being from  $\frac{1}{15}$  to  $\frac{1}{10}$  of a grain or, in strong individuals, even  $\frac{1}{5}$  of a grain; sedative effects may be obtained with  $\frac{1}{25}$  to  $\frac{1}{30}$  of a grain. As a rule the use of apomorphine should be avoided in children, in whom it nearly always acts badly.

In the treatment of periodical dysmaniacs and in all acute cases of alcoholism Rosenwasser advises  $\frac{1}{10}$  of a grain of apomorphine hypo-

<sup>1</sup> Deutsch. med. Wochenschrift., 1906, xxxii, 16.

<sup>2</sup> Medical Record, July 27, 1907.

<sup>3</sup> Ibid., p. 20.

dermically, to which  $\frac{1}{80}$  of a grain of strychnine is added, if the heart is acting poorly. The patient should be lying down and basins should be in readiness owing to the rapid action of the drug. Within a few minutes after vomiting has occurred the patient falls asleep and may sleep from two to eight hours. In most instances he awakes refreshed, sober, and rational.

Rosenwasser states that he has never failed to obtain the hypnotic effect in alcoholics and but once did the drug fail as an emetic. In many cases  $\frac{1}{80}$  of a grain is sufficient or this small dose may be given in the course of a few hours to prolong the effect of the original dose. Bromides, chloral, or other sedative drugs if used later are generally effective in a much smaller dose after apomorphine has been used.

The drug should not be given by mouth in these cases, as it is uncertain in its action. Indeed, one of the great advantages claimed for it in alcoholics is that it can be given without objection on the part of the patient when he will obstinately refuse to take medicine by mouth.

**Belladonna.** In the treatment of *nocturnal enuresis* in children, Still<sup>1</sup> advises the use of tincture of belladonna. Inasmuch as threadworms are not unusually the cause of the enuresis, Still advises giving 1 to 2 grains of santonin, to be followed by calomel, in order to make this point sure. He gives as an initial dose 5 minims of the tincture of belladonna to children beyond infancy; for a child five years of age or older the initial dose should, as a rule, be 10 minims. The dose is increased  $2\frac{1}{2}$  minims every fifth or sixth day until the enuresis is stopped or the point of tolerance is reached. The minimum effective dose should then be continued for two weeks. The dose is then diminished  $2\frac{1}{2}$  minims a week and so gradually discontinued. If, after the drug has been pushed up to 20 minims with but partial control of the enuresis and a farther increase of the belladonna produces alarming symptoms, Still combines with it the tincture of lycopodium (12 minims increased to 20 minims), tincture of nux vomica, potassium bromide, or phenacetin.

Belladonna has long been used in the treatment of enuresis, with results far from satisfactory. It not infrequently fails altogether and, even when it causes a disappearance of the enuresis, the effect is rarely curative. The management of these cases requires an infinite amount of patience. Harsh measures should be absolutely prohibited. An examination of the urine is most essential. If it is concentrated and highly acid, alkaline diuretics are indicated. An efficient mixture is one containing potassium citrate and sweet spirit of nitre. As the urine increases in amount and becomes clearer, small doses of tincture of belladonna may be added, but care should be taken to see that the belladonna does not diminish the quantity of urine, as concentrations may again result.

<sup>1</sup> Clinical Journal, April 24, 1907

In the event of the urine being concentrated and alkaline in reaction, with a strong ammoniacal odor, the indication is to acidify it. The drugs most efficient for this purpose are urotropin in 4-grain doses three times a day or benzoate of ammonium in the same doses. If these measures fail the trouble may be due to weakness of the spinal centres governing the bladder. In such cases arsenic and strychnine are indicated.

Still also referred to *ergot* in 20- to 30-minim doses three times a day. In very obstinate cases this might be tried. The sedative action of ergot is very marked, according to Eustace Smith,<sup>1</sup> who has employed it in the treatment of *chorea*.

**Bicarbonate of Sodium** has been used for years for the relief of gastric pain and hyperacidity of the stomach.

According to Meunier<sup>2</sup> sodium bicarbonate has been used in cases of *gastric pain* on the following theory: The gastric pain is due to an excess of hydrochloric acid, which causes no inconvenience during digestion owing to its absorption by the food. When the stomach is empty the acid begins to exercise an irritating action upon the sensitive nerves of the mucous membrane. The administration of sodium bicarbonate at an interval of two, three, or four hours after a meal results in relief of the pain. Meunier has tested the validity of this theory both clinically and chemically. He found that in nearly every one of sixteen cases pain was most severe when the secretion of hydrochloric acid was at a minimum. Inasmuch, however, as pain was nearly always relieved by sodium bicarbonate, Meunier was led to ascribe its good effect not to any neutralizing action, but to the production of carbon dioxide, which exerts a calmate effect on gastric pain. If this hypothesis is correct, Meunier believes the administration of sodium bicarbonate alone is a poor method of producing the carbon dioxide, inasmuch as its therapeutic action is proportional to the quantity of hydrochloric acid present and is liable, therefore, to great variation. Additional objections are that neutralization of the hydrochloric acid retards digestion, as pepsin acts only in an acid medium; furthermore, the investigations of Pawlow have shown that the acidity of the gastric juice is the specific excitant of the pancreatic gland.

Meunier, therefore, suggests that the carbon dioxide be produced by means of tartaric acid and a mixture of carbonates given so as to slowly and continuously evolve the gas without modifying the acidity of the gastric juice. For this purpose he advises that the tartaric acid be prescribed in 1-gram (15-grain) powders and the carbonate powders be made up of sodium bicarbonate 0.4 gram (6 grains), calcium carbonate 0.3 gram (4½ grains), and hydrated magnesium carbonate 0.2 gram (3 grains). The patient is directed to add an acid and an alkaline powder separately, each to half a glass of water, and, when the pain begins,

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1904, p. 323.

<sup>2</sup> Bulletin des sciences pharmacologiques, 1906, No. 10; Lancet, January 19, 1907.



to take alternately tablespoonful doses of the acid and the alkaline mixtures. Clinically he has found that this plan is much more efficacious in relieving the pain than is sodium bicarbonate alone.

**Bromoform** is one of the many remedies that has been employed in the treatment of whooping-cough. Two years ago several instances were recorded in which severe poisoning occurred in children who were being given bromoform. The untoward effects in these cases were due, not to any especial susceptibility on the part of the children to the bromoform, but because of the fact that the bromoform settled at the bottom of the mixture. Thus, while the doses from the upper part of the bottle contained no bromoform, a large, concentrated dose was given when the lower part of the mixture was reached. This fact should be borne in mind and, if bromoform is prescribed, it should be seen that the bottle is thoroughly shaken before each dose. Benson<sup>1</sup> has recently reported an instance of bromoform poisoning. In his case the child was receiving a mixture containing one-minim doses of bromoform for the relief of whooping-cough. While he fails to mention the number of doses given, it is quite probable that the untoward effects were produced in the manner described above.

**Cactus Grandiflorus** enjoys the reputation of being a good substitute for digitalis in certain cardiac disturbances. Inasmuch as cactus grandiflorus was voted out of the official list in the last edition of the *U. S. Pharmacopœia*, Sayre<sup>2</sup> undertook to determine its medicinal value. The first difficulty he encountered was in obtaining a supply of reliable material. Sayre's results indicated that the cardiac action of the drug was slight and uncertain. Samples submitted to E. M. Houghton were reported by the latter to have so slight a physiological action that it might be considered as practically *nil*. Sayre thinks that the drug should be denied official recognition because of the uncertainty of the supply of reliable material, the difficulty in identifying the material, and the fact that the fresh drug rapidly deteriorates.

Hatcher<sup>3</sup> also condemns cactus grandiflorus as being inert and absolutely useless. In regard to *cactin* or *cactina*, the so-called active principle of cactus grandiflorus, Hatcher states that these two preparations are not only devoid of a digitalis or a strychnine-like action, which has been claimed for them, but that they are inert when used on animals in doses that are hundreds, and even thousands, of times as large as those recommended by their exploiters.

**Ohloral Hydrate.** The use of this drug in the treatment of *scarlet fever* was first advocated by J. C. Wilson some twenty years ago, but has never met with general acceptance. Recently, Royer<sup>4</sup> has submitted

<sup>1</sup> British Medical Journal, June 27, 1907.

<sup>2</sup> Therapeutic Gazette, December 15, 1906.

<sup>3</sup> Journal of the American Medical Association, September 21, 1907.

<sup>4</sup> Therapeutic Gazette, January, 1907.

the drug to an extensive trial at the Philadelphia Municipal Hospital. The claims made for chloral in the treatment of scarlet fever are that it in some way protects the functioning part of the kidney tissues; that the nervous symptoms are greatly modified; that the itching is allayed, and that the patient is made more comfortable. Royer is of the opinion that the drug does fulfil all of these conditions. He was not able, however, to confirm Wilson's claim that it increased diuresis.

Ever since chloral has come into general use the belief has been strong that the drug was a marked cardiac depressant. Royer states that the cases to which he administered the drug were studied particularly from this standpoint. "After having treated nearly a thousand patients with doses of sufficient size to produce light somnolence, we feel that chloral hydrate does not materially depress the circulation. We believe that in no instance did the drug act clinically as a serious depressant. After having a larger experience we rarely discontinued its use, no matter what the degree of depression might be."

The depressant effect of chloral has, quite possibly, been overestimated, but the belief is so strong that I think most would hesitate to use it when marked depression of the circulation was already present. Under these circumstances small doses of the tincture of digitalis might be combined with the chloral.

The object of the chloral treatment in scarlatina is to administer the minimal amount of the drug necessary to produce light and continued somnolence. The dose, of course, must be adjusted to the age and requirements of each individual case. Wilson recommends the following formula for the administration of the chloral:

R—Chlorali hydrati . . . . . gr. xxx  
 Syrupus lactucarii (Aubergier),  
 Aquæ dest. . . . . ʒss vel fʒj—M.

Sig.—A teaspoonful in iced water every two, three, or four hours, if possible after food.

This method of treating scarlatina is probably best adapted to cases in which the nervous symptoms are very pronounced.

Hatcher<sup>1</sup> has made a comparative study of the action of chloral hydrate and *isopral*. The latter preparation was introduced as being a much safer hypnotic than chloral. Hatcher states that his experiments on rabbits and cats and those of Impen's on rabbits showed that there was no essential difference between the action of *isopral* and hydrated chloral in effective doses on the respiratory centres. Furthermore, his experiments on dogs showed that *isopral* was more than twice as active in depressing the vasomotor and respiratory centres and the heart.

Another preparation which has been introduced as "just as good as chloral" and free from the dangers of that drug is *somnos*. It has been

<sup>1</sup> Medical Record, May 25, 1907, p. 877.

shown that if somnos does not depend on chloral for its hypnotic effect it at all events possesses an action in no way differing from that substance.

Beates<sup>1</sup> reports two cases of the somnos habit. An overdose of somnos produced symptoms in one case identical with those seen after an overdose of chloral. An unusual untoward effect following the use of chloral has been reported by Gregor.<sup>2</sup> A woman, suffering from paranoia, accompanied with marked motor excitability, was given two doses of chloral hydrate twenty-four hours apart. The second dose was followed by an eruption covering most of the body. It consisted of dark-red maculopapular lesions, which in places were hemorrhagic. In addition large bullæ filled with serous fluid developed about the face. The eruption was accompanied by a rise in temperature, marked somnolence, and hemorrhagic bronchitis and conjunctivitis.

It is known that susceptible persons sometimes develop redness and swelling of the conjunctiva after taking chloral. At times this untoward effect is noticed only after alcohol is simultaneously taken with the chloral. Chronic chloralism sometimes produces an erythematous, papular, urticarial, vesicular, or petechial eruption. The present case is of interest from the fact that the eruption was apparently produced by two doses.

**Chloretone.**—Because of its local anesthetic effect chloretone is useful in painful and irritable conditions of the stomach. Wynter<sup>3</sup> recommends chloretone in 5- to 10-grain doses for the relief of pain due to *gastritis*, *gastralgia*, *gastric cancer*, and *gastric ulcer*. In addition to relieving the pain, chloretone also favorably influences vomiting and fermentation; it has been very efficient in preventing postanesthetic vomiting. *Vaginal pruritus* is sometimes relieved by the local application of a 0.4 per cent. solution of chloretone in warm water.

Wynter speaks especially of the value of chloretone as a preventive of *seasickness* and in the management of *chorea*. When used to prevent seasickness the drug is given in 5-grain doses about twenty minutes before meals, two or three times a day during rough weather. Children suffering from *chorea* were greatly benefited by chloretone. Wynter has treated fourteen cases of *chorea* in the following way: Five grains of chloretone in half an ounce of petroleum emulsion were given three times a day for two and sometimes three days; there was in all of them such a marked diminution of the choreic movements that the dose was then halved and sometimes given only twice and even once a day, according to the severity and progress of the case. The time during which the chloretone was used varied from five to ten days. After the choreaform movements were controlled iron, arsenic, and cod-liver oil were given. Under the influence of the drug the movements rapidly

<sup>1</sup> Journal of the American Medical Association, June 29, 1907.

<sup>2</sup> Münchener med. Wochenschrift, April 23, 1907.

<sup>3</sup> Lancet, March 30, 1907.

ceased. The stay in the hospital averaged three weeks for the fourteen cases. Wynter is uncertain as to the permanency of the results. The only untoward effects noticed were exfoliation of the skin on the hands and heels in two cases, and in two others marked somnolence due, no doubt, to the drug being given in too large doses.

It should also be mentioned that chloretone is of service as a hypnotic under the same conditions as chloral. As chloretone has no depressing effect on the heart or respiration, it is preferable to chloral in conditions associated with a weak heart. Wynter prescribed the drug in the form of a powder, or in an emulsion of petroleum. It may also be given in tablet form (3 to 5 grains each). The dose is from 5 to 20 grains.

**Chloride of Sodium.** Attention has been called, in previous numbers of *PROGRESSIVE MEDICINE*, to the role played by sodium chloride in the production of the edema associated with chronic *nephritis*, particularly of the parenchymatous type. By "dechloridization therapy" is meant the entire withdrawal, or the reduction to a minimum, of all salt artificially added to the food. Peabody<sup>1</sup> has reported favorably on this method of treating nephritis. His best results were obtained in cases of general anasarca from chronic parenchymatous nephritis. In anasarca due to heart causes or to combined failure of heart power and interstitial nephritis the withdrawal of salt accomplished very little.

The dietary recommended by Peabody is as follows:

*Breakfast.* Coffee or tea, eggs, cereals, cream, fresh butter, fruits, bread made without salt.

10 A.M. A glass of milk.

*Dinner.* Chicken, fish, potato variously prepared, bread made without salt, ice-cream, jelly, fresh butter, cocoa  $\mathfrak{F}$ viiij.

3 P.M. A glass of milk or water.

*Supper.* Eggs, chicken, bread without salt, jelly, custard, cream, fresh butter, tea  $\mathfrak{F}$ viiij.

8 P.M. A glass of milk or water.

Almost any kind of meat or vegetable can be given to which salt is not added. Peabody states that the unsalted bread has proved to be very palatable, especially if made with milk instead of water.

In regard to the rest of the treatment, there was some reduction in the quantity of fluids ingested, but this was not carried to the point of making the patient uncomfortable.

Of the heart tonics Peabody states that digitalis, and theobromine, in the form of diuretin, are to be preferred, although he is rather skeptical as to whether they really do any good, for in none of the cases was the blood pressure raised. He used hot-packs in a few instances and catharsis in others. Inasmuch as very little sodium chloride is elimi-

<sup>1</sup> Medical Record, March 9, 1907.

nated by the skin and catharsis cannot be kept up very long, Peabody does not attach much importance to these aids. Colonic irrigations with hot water, to which sodium bicarbonate had been added ( $\frac{1}{2}$  oz. to the pint), were of benefit. As water alone is irritating to the mucous membrane of the gut, the density of the water must be raised by some such substance as the bicarbonate of sodium. The usual sodium chloride solution is not used for obvious reasons.

In the discussion of Peabody's paper it was agreed that even if this method of treatment was not curative the temporary relief afforded was of great benefit. Observations as to the permanency of the results and the effect of again resuming a salt diet are too meager to allow of any conclusions.

The beneficial effects of a milk diet, in treating nephritis, are now believed to be due to the low sodium chloride content of milk. For some time it has been the practice of French clinicians to keep scarlet-fever patients on a milk diet, in some instances for as long a period as forty days. Even if scarlatinal nephritis is due to some secondary infection settling in the kidneys, the use of a milk diet, while it may not prevent the occurrence of the nephritis, will at least tend to relieve the extra strain thrown on the kidneys. It is now thought that equally good results may be obtained by using a varied diet free from the artificial addition of salt.

While the general trend of opinion seems to be favorable to "dechloridization therapy" there is not a general agreement on the subject. Thus Bittorf and Jochmann<sup>1</sup> report a study of the metabolism, with and without salt in the food, in fourteen cases of kidney or heart disease, or both. They are of the opinion that changes in the vessel walls are responsible for the edema and not the retention of the chlorides. For this reason dechloridization, as a method of treating kidney affections, is unscientific, except in so far as the diet is rendered more easily digested and assimilable. An excellent analysis of the theory of chloride retention will be found in an editorial article in the *Journal of the American Medical Association*, April 12, 1907. It is here stated that the weight of evidence is all in favor of the view that nephritic edema is due, primarily, to the retention of sodium chloride, the retention of water being secondary in order that the chlorides in the tissues may be kept in solution. The article closes as follows:

"In any case, however, the treatment of renal dropsy by 'dechloridization therapy' seems to be warranted on several grounds. In the first place, of course, comes the indication that in many cases edema is relieved by this means; the amount of chlorides excreted on a chloride-poor diet being much in excess of the amount taken in, such a diet soon leads to removal of the retained chlorides and with them the retained water.

<sup>1</sup> Deutsch. Archiv f. klin. Med., 1907, lxxxix.

Secondly, there is considerable evidence that chlorides may act injuriously on the diseased kidneys; indeed, excessive quantities of sodium chloride may cause albuminuria even in healthy individuals, which observation suggests the possibility that the use of over-salted foods may be an important factor in the production of nephritis. It seems to have been commonly found that nephritic patients kept on a chloride-poor diet show a decreased amount of albumin in the urine, while administration of chlorides causes it to increase. Furthermore, there is abundant evidence that there is no danger in reducing the intake of chlorides to as low a figure as can be done by a carefully selected diet. To reduce the chlorides to such a reasonable minimum, say from 2 to 3 grams a day, no very difficult procedures are necessary, for in eggs, unseasoned meats, and unsalted butter we have foods that are nearly salt-free, while the salt content of milk is very low. Bread without salt, fresh-water fish, potatoes, rice, fresh vegetables, fruits, and chocolate offer a considerable variety of salt-poor foods that make the regulations of a dechloridization diet not intolerable to the patient.

It may be added that Widal insists on repeated weighing of the patient, in order to keep track of the degree to which the water is being removed during the treatment."

It is to be borne in mind that while some cases of interstitial nephritis may be benefited by "dechloridization therapy," the best results are obtained in chronic parenchymatous nephritis.

Massalongo and Zambelli<sup>1</sup> have applied the salt-free diet in the management of chronic cardiac affections. From a study of their own cases and a review of the literature they conclude that sodium chloride plays a very important part in the phenomena of asystoly and in the production of the edema of cardiac incompetence. Retention of sodium chloride is a constant phenomenon during failing compensation, and this retention is accompanied by dropsical accumulations in the tissues. In some cases the mere reduction of the amount of salt ingested is sufficient to restore the cardiac balance; in others diuretics and heart tonics were used to accelerate the effect. They found that the restriction of salt was an excellent means of determining the functional condition of the heart, both for diagnosis and prognosis. The use of diuretics and heart tonics alone did not give as good results as when the salt-free diet was also employed. Enriquez and Ambard<sup>2</sup> advise the use of a salt-free diet in the treatment of *bradycardia*. They report a case in which the pulse rate increased from 32 to 72 beats within a period of seven weeks, the only measure employed being the withdrawal of salt from the food. The reason given for this effect is that in these cases there is usually a chronic nephritis with retention of the chlorides. As a result of this

<sup>1</sup> La Riforma Medica, December 8, 1906.

<sup>2</sup> Semaine médicale, 1907, No. 4.

retention, the myocardium is constantly bathed in a hypertonic solution, which interferes with its proper functions. It is difficult to understand how this treatment would in any way influence cases of bradycardia associated with a gross lesion in the bundle of His. The trouble in such instances is that the normal fibers making up this bundle are entirely or in part destroyed. Certainly the reduction of chlorides or any other treatment would have very little effect in such cases. The value of a salt-free diet in the management of cardiac affections is, after all, of doubtful value. Peabody<sup>1</sup> obtained no results whatever in such cases.

Gordon<sup>2</sup> has treated thirty-seven cases of epilepsy with a salt-free diet. The claim, that by such a diet the bromides can be increased and the number of seizures lessened, has not been generally accepted.

**Coley's Fluid.** The treatment of inoperable sarcoma, by means of the mixed toxins of erysipelas and *Bacillus prodigiosus*, was first advocated by Coley<sup>3</sup> fourteen years ago. During the past eighteen months he has published two additional papers on the subject.<sup>4</sup>

The clinical observation, that an attack of erysipelas had a retarding effect on a sarcomatous growth, led Coley to treat inoperable cases of malignant growths with living cultures of erysipelas. His early results showed two things: first, that it was a difficult matter to produce erysipelas when desired, and, second, there was considerable danger of the patient dying from the artificially produced erysipelas. Later he found that an inhibitory action could be obtained by sterilizing the cultures with heat, but that this method was insufficient to control the tumor growth. Acting on Roger's assertion that the virulence of the streptococcus of erysipelas could be greatly increased by growing the *Bacillus prodigiosus* with it, Coley was led to use the mixed toxins of these two organisms.

Tracy<sup>5</sup> has recently published some experiments on the effect of these toxins. She studied the effect of the toxin of the streptococcus alone, of the *Bacillus prodigiosus* alone, and of the combined toxins, upon sarcoma in dogs. From these experiments she was able to demonstrate that the *Bacillus prodigiosus* alone had the power of causing the entire disappearance of rapidly growing sarcomas in dogs and their apparent cure. She, furthermore, found that the mixed toxins of erysipelas and *Bacillus prodigiosus* caused even a more rapid disappearance of the tumor than the *Bacillus prodigiosus* alone. She was also able to show that the disappearance of the tumors, under the influence of the toxins, was due to an increased leukocytosis and coagulation necrosis.

<sup>1</sup> Loc. cit.

<sup>2</sup> Pennsylvania Medical Journal, 1907.

<sup>3</sup> American Journal of the Medical Sciences, 1893.

<sup>4</sup> Ibid., March, 1906; Medical Record, July 27, 1907.

<sup>5</sup> Journal of Medical Research, 1907, xvi, No. 2.

Dr. Tracy in addition has devised a new method of preparing the toxins. Coley states that the toxins as prepared by Tracy are not only more powerful but more efficient than those he has previously used. For details as to her method of preparing the toxins the original article should be consulted. Coley gives the following directions for using the toxins:

"It is most important to begin in every case with a very small dose, not over  $\frac{1}{4}$  minim (diluted with a little boiled water to ensure accuracy of dosage). If the tumor in question is highly vascular, it is wiser to begin the injections remote from the same, until the susceptibility of the patient to the toxins has been ascertained. This varies considerably in different individuals. After a few doses it is safe, in most cases, to inject into the tumor itself.

"As a rule, when giving injections into the tumor, only about one-fifth of the dose used for injections remote from the tumor is required to produce the same reaction. The dose should be increased by  $\frac{1}{4}$  minim when given into the tumor; by  $\frac{1}{2}$  minim when injected remote from the tumor, until the desired reaction is obtained. The best results are obtained by doses sufficiently large to produce severe reactions, say a temperature of  $102^{\circ}$  to  $105^{\circ}$  F.

"The frequency of the injections must depend entirely upon the strength of the patient, some being able to bear daily injections, while in others it may be unwise to push the treatment beyond three or four injections a week.

"In the successful cases the effect is usually very promptly noticeable. The tumor becomes smaller in size, much more movable, and very much less vascular. These changes appear very quickly, often within two to three days.

"The action of the toxins is both local and systemic. Sometimes the best results are obtained by giving the injections alternately into the tumor and remote from the same. In tumors in inaccessible regions, *e. g.*, intra-abdominal sarcoma, or sarcoma of the tonsil, a perfect cure may be obtained entirely by systemic injections."

Coley has now treated 42 cases. Of these cases 17 were round-celled sarcoma, 17 spindle-celled sarcoma, 2 mixed-cell sarcoma, 1 chondrosarcoma, and 1 epithelioma. The late results in these cases are as follows: 21 well from five to fourteen years, 26 well from three to fourteen years, and 10 well from ten to fourteen years. In addition to these cases other surgeons have reported to him successfully treated cases, bringing the total number to nearly 100. Bloodgood (see p. 217) is very skeptical as to the value of the mixed toxins, and his opinion is probably shared by the majority of surgeons. Coley's report, however, is so favorable that it would seem advisable to give the mixed toxins a thorough trial in order that their value may be definitely settled one way or the other.



**Cotarnine.** The value of cotarnine as a *uterine hemostatic* was called attention to, by Norris,<sup>1</sup> two years ago. v. Ramdohr<sup>2</sup> also highly praises the drug. Cotarnine is a derivative of narcotine. The phthalate of cotarnine (styptol) seems to be the most satisfactory salt. It is a yellow, crystalline powder, readily soluble in water, and it is administered in doses of  $\frac{1}{2}$  grain, three or four times daily. So far no toxic effects have been observed.

**Creosote** has long been employed in the treatment of *pulmonary tuberculosis*. At the present time the drug is enthusiastically recommended by some and severely condemned by others. The advocates of creosote claim that no single drug is so generally useful in the treatment of pulmonary tuberculosis, while its enemies blame it for countless cases of disordered stomachs.

Bouchet<sup>3</sup> recommends that creosote, when given in capsules, should be administered on a full stomach, in order to prevent an irritant effect on the mucous membrane. He advises the use of powdered charcoal as a diluent. Failure to obtain results with creosote, in pulmonary tuberculosis, is largely due to its use in too small doses and its administration in a concentrated form. For the past three years I have used creosote rather extensively in the treatment of pulmonary tuberculosis, associated with severe cough and profuse expectoration. The drug is best given as follows: For each drop of the creosote there should be a tablespoonful of hot water. The creosote should then be thoroughly emulsified by actively stirring with a spoon for at least five minutes. As the larger doses are reached (15 to 20 drops) the amount of water need not exceed a tumblerful; with the larger doses a rapid and thorough emulsification can be obtained by the use of a lemonade shaker. The creosote is given fifteen to twenty minutes before meals. When prepared in this way, as much as 20 drops can be given, three times daily, for weeks or months. The claim that creosote has an injurious effect on the kidneys is not supported by clinical experience. In the treatment of gastrointestinal disorders small doses of creosote may be used to advantage. As an *intestinal antiseptic* Skinner<sup>4</sup> recommends the following formula:

R—Creosoti . . . . .	℥iij
Tr. capsici . . . . .	℥v
Tr. nucis vomicæ. . . . .	℥vij
Elix. calisayæ . . . . .	q. s. ad f℥j.—M.

Sig.—To be taken at one dose.

He also recommends doses of from  $\frac{1}{10}$  to 1 minim in the *acute diarrheas of infancy and childhood*.

As substitutes for creosote, Skinner mentions *guaiacol* and *guaiacol*

<sup>1</sup> PROGRESSIVE MEDICINE, September, 1905, p. 263.

<sup>2</sup> New York Medical Journal, March 9, 1907.

<sup>3</sup> Progrès médicale, September, 1906.

<sup>4</sup> Mississippi Medical Record, 1906.

*carbonate*. I have used the latter a great deal during the past year, after the formula recommended by Jacobi,<sup>1</sup> but I have not been able to reach the doses he advises (10 to 20 grains t. i. d.). In 5-grain doses, combined with nitrate of strychnine, arsenic trioxide, and sparteine sulphate, cough and expectoration have been materially lessened and little or no stomach disturbance has occurred.

**Diet.** The increase in the number of articles dealing with the dietetic management of disease indicates that this subject is gradually assuming the importance it deserves. At the present time the importance of dietetics is too little emphasized in the medical schools, and too little appreciated by the profession at large. Lack of knowledge on the subject of dietetics has led many to place their main reliance on the "*medicinal foods*." The statements of the manufacturer have been blindly accepted and the simple preparations that are easily and cheaply made in the home are neglected.

The Council of Pharmacy and Chemistry of the American Medical Association<sup>2</sup> has done a praiseworthy work in investigating the nutritive value of a number of these predigested foods. The results are so interesting and important that they should receive as much publicity as possible.

"In order to get a fair conception of the actual food value of these various preparations, it is desirable to make some comparison which can be readily comprehended by every physician. The amount of good milk necessary each twenty-four hours to sustain the vitality of a patient during a serious illness is not less than 64 ounces, or approximately 2000 c.c. The food value in calories represented by this amount of good milk may be placed at 1430. This includes not only the proteid and carbohydrate matter, but the fat as well. By comparing this available potential energy with the total energy available in the predigested foods under consideration, it can be readily seen that if a physician depends on the representations made by some of the manufacturers, and feeds his patient accordingly, he is resorting to a starvation diet. . The largest number of available calories, including alcohol, present in any of the recommended daily doses, is less than one-fifth of the number of calories represented by 2000 c.c. of milk; and the calories represented by the daily dose of the preparation poorest in food products is only one-twenty-fifth of the amount present in 2000 c.c. of milk. These figures tell their own story.

"Making 2000 c.c. of milk the basis of calculation, and estimating the amount of the various preparations required to yield this number of calories, it is found that the quantity to be administered daily to supply 1430 calories, including alcohol, varies from 716.2 to 1506.2 c.c. In other words, it will be necessary, in order to supply 1430 units of energy

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906.

<sup>2</sup> Journal of the American Medical Association, May 11, 1907.

*per diem*, to administer the amount of the various products in quantities found within the above limits. In many cases the amount of *alcohol* exhibited by these quantities would keep the patient in an alcoholic stupor continually. The cost necessary to supply this energy varies from \$1.48 to \$3.39. Compare these prices with the cost of two quarts of milk. Is farther comment necessary?"

Edsall,<sup>1</sup> in commenting on the Council's results, states that it has been his observation that the common use of the medicinal foods largely depended on three factors:

1. Their nutritive value is thought to be very great. Often, indeed, it is believed that the very few ounces that can be given provide a reasonably large day's ration. Edsall says that he has repeatedly had occasion to calculate the actual colorific value of the day's ration of patients whom he found using these foods, by the advice of their physicians, as a more or less considerable part of their diet. In such instances he found, almost as a rule, that they were taking, at most, one-third of what they actually required in order to maintain nutrition; usually it was less than this. One of the most serious things these patients suffer from is more or less severe starvation. Edsall states that he is convinced that many a patient has suffered severely when preparations such as these have been used, and that not a few of them have died chiefly of starvation.

2. A not uncommon cause of the use of these preparations is the fact that it is easy to remember the names of a number of these medicinal foods, while it takes more trouble to acquire a knowledge of a variety of simple and cheap preparations that can be readily prepared in the home.

"Much of the use of these foods depends simply on imperfect teaching in dietetics."

3. It is frequently believed that the medicinal foods are often borne by a disordered digestive tract when other foods are not. Edsall is of the belief that this is a very erroneous view and that a very moderate degree of skill and resource in using simple home-made preparations renders the temptation to use "prepared foods" very slight.

In his opinion medicinal foods have but one limited sphere of usefulness, namely, in very capricious patients with an uncertain appetite and an irritable digestion. In such cases variety is frequently essential in addition to the necessity of providing an adequate amount of nourishment. Edsall states, however, that such cases are, after all, rare, and that an equal amount of time and care spent on learning the varieties of home preparations, as is given to trying various proprietary foods, will give infinitely better results.

In regard to the alcohol content he writes: "Would it not be utterly irrational to be obliged to give a small dose of strychnine, for instance,

<sup>1</sup> Journal of the American Medical Association, May 18, 1907.

with each small portion of food; and to be obliged also, every time that one increased the food, to increase coincidently from one to five times the amount of strychnine that one was giving?" The alcohol content in these foods is particularly emphasized by the Council. Aside from the possible intoxicating effects of the alcohol, even small doses irritate the stomach and may be disadvantageous in other ways, particularly in nervous cases.

It was at one time the almost universal belief that the attainment of strength and endurance largely depended on red meat. The training table of athletes of twenty years ago is an illustration of this theory. At that time, and indeed down to a much later period, rare meat was given at least twice and not infrequently three times a day. To the best of my knowledge, such views are no longer held by trainers, and it is now recognized that a liberal mixed diet is capable of giving the best results.

Some experiments recently conducted by Professor Irving Fisher, of Yale University,<sup>1</sup> on the relation of endurance and diet, are of interest. The endurance tests were three in number: holding the arms horizontally, deep knee bending, and leg raising. The subjects tested were divided into three groups: (1) Athletes accustomed to a high-proteid and full-flesh dietary; (2) athletes accustomed to a low proteid and non-flesh dietary; and (3) sedentary persons accustomed to a low-proteid and non-flesh dietary. Of the meat abstainers they had been without flesh food for periods varying from four to twenty years, and some had never taken meat at all.

The following table shows the results to be all in favor of the vegetarians:

	Arm holding.		Deep knee bending.		Leg raising.	
	Number of persons	Average record. Minutes.	Number of persons.	Average record. Times.	Number of persons.	Average record. Times.
Flesh eaters, athletes . .	15	10	9	383	6	279
Abstainers, athletes. . .	19	39	16	927	6	288
Abstainers, sedentary. .	13	64	5	535	1	74

While these tests are extremely interesting, they are somewhat defective in that there was no class made up of moderate meat eaters. The athletes accustomed to meat had this article of food two or three times a day and for that reason could hardly have been classed as temperate users of meat. In considering the most suitable diet for the average man it is undoubtedly true that a mixed diet is the best.

<sup>1</sup> Yale Medical Journal, March, 1907

Bornstein<sup>1</sup> is not a believer in the superstition that meat has a special value as a strength giver. In addition he states that meat contains substances that lead to the formation of uric acid and increase putrefactive processes in the intestine, leading to auto-intoxication. For this reason meat is especially contra-indicated in neuralgias dependent on auto-intoxication. Bornstein advises that meat be used, in limited quantities, in the treatment of *neuritis*, *rheumatism*, *hysterical manifestations*, *neurasthenia*, and *exophthalmic goitre*. The amount of meat should also be limited in *cardiac affections*. He reduces the amount of meat to a minimum in diabetes and substitutes for it albumin in the form of albumin of milk, generally some form of casein, to which he adds small doses of iron and quinine. Bornstein attributes a large proportion of the nephritic processes in diabetes to the use of alcohol and meat. Red meat was, at one time, largely forbidden to nephritic patients, but, as was pointed out in last year's review, a more liberal view now prevails and red meat is held by many to be no more injurious to these individuals than the white meats.

Bornstein also holds that as the extractives of meat stimulate gastric secretions, meat should be totally avoided in the treatment of *gastric ulcer*. This view is not in accordance with the method of treatment advocated by Lenhartz.

The Lenhartz<sup>2</sup> treatment of gastric ulcer is as follows: Starting with 2 eggs and 6 oz. of milk on the first day, he increases the eggs 1 a day until 8 are taken and continues at this number, the milk being simultaneously increased 3 oz. a day until a quart is taken and continued at this amount. The eggs and milk are given ice cold and in teaspoonful doses. On the third day  $\frac{3}{4}$  oz. of sugar is given, and this is gradually increased until, on the ninth day, 1.6 oz. are given, and this amount continued. On the sixth day 1 oz. of raw, scraped beef is given, double this amount on the next day, and so continued. On the seventh day 3.3 oz. of milk, cooked with rice, are added and gradually increased to 2 oz. on the eleventh day. On the eighth day  $\frac{3}{4}$  oz. of zweibach is added and gradually increased until 3.3 oz. are given on the fourteenth day. On the tenth day 1.6 oz. of raw ham are given and continued daily in this amount. Butter is also added on the tenth day, giving  $\frac{3}{4}$  oz. and double this amount on the next day and continued.

Steele in commenting on this method, two years ago, stated that it was growing in favor. Thesen<sup>3</sup> agrees with Lenhartz that it is not necessary to starve patients suffering from gastric ulcer. He also agrees with those who advocate rest for the ulcerated stomach. He reconciles these views by assuming that the food cannot directly induce pain in the

<sup>1</sup> Therapie der Gegenwart, 1906, Nr. 5.

<sup>2</sup> Alexander Lambert, Trans., Section on Medicine, American Medical Association, June, 1906.

<sup>3</sup> Abst., Journal of the American Medical Association, May 18, 1907.

stomach, and that direct irritation has only a very mildly deleterious influence on the ulcer.<sup>1</sup>

Thesen is of the opinion that, in order to prevent unnecessary movement on the part of the stomach, the food should be given in small quantities and at frequent intervals, not more than 15 to 100 c.c. at a time. He states that the foods which excite stomach peristalsis least are the white of an egg, raw scraped beef and fish, butter and cream. He restricts the dietary to these.

Kohnstamm<sup>2</sup> cautions against the use of meat in individuals habitually constipated. For such patients he advises a liberal supply of milk and butter. In regard to milk many patients complain that it makes them constipated. While this is often true of small quantities (2 to 3 glasses a day) it has been my experience that large quantities (2 to 3 qts. a day) rarely cause constipation.

In a consideration of the most economical diet for the aged poor, dependent on state aid, Landouzy<sup>3</sup> states that meat is too costly and is, besides, less nourishing than other articles of food. He suggests that a suitable and inexpensive dietary can be made up from bread, a little ham or bacon, grapes or raisins, chocolate, vegetables, rice, and cheese. Soup can be made from vegetables and bacon fat. They may be allowed milk or coffee. It is to be borne in mind that in those of advanced years but few calories need be expended for muscular energy; most of the caloric energy is expended in maintaining the body heat. To the objections already advanced against an excessive meat diet, Reyburn<sup>4</sup> adds another. He believes that the excessive consumption of nitrogenous or animal foods is a factor in the production of cancer. In regard to this point he calls attention to the following facts: (1) Cancer is comparatively rare in hot climates, and especially where the diet of the inhabitants is composed chiefly of rice or other starchy food. (2) Cancer is very prevalent at the present time wherever animal food is largely consumed; the number of cases of cancer has been found to increase in proportion to the increase in the consumption of nitrogenous or animal foods. Reyburn agrees with Landouzy that individuals of advanced years are not in the same need of food as younger persons, as their expenditure of energy is so much less. Sir Henry Thompson is quoted as stating that in fifty years of practice he had rarely seen cancer (except of the lip) in those who labor in the open air. He ascribes this to the fact that waste materials produced in the body are burned up by hard manual exercise.

The choice of diet in the management of *pulmonary tuberculosis* was fully considered in last year's review.<sup>5</sup> If not the most important

<sup>1</sup> See p. 57 in present volume.

<sup>2</sup> *Presse médicale*, 1907, No. 5.

<sup>3</sup> *Journal of the American Medical Association*, November 10, 1906.

<sup>5</sup> *PROGRESSIVE MEDICINE*, December, 1906.

<sup>4</sup> *Ibid.*

factor in treating this disease it certainly merits as much attention as the selection of a suitable climate, the regulation of exercise, or the giving of medicine. Personally, I would rank it first. The essential points in dietary management of the consumptive patient may be briefly stated as follows: The ingestion of foods capable of producing an increase in weight; milk and eggs are more nearly ideal for this purpose than any other food. Specific directions should be given as to the amount and the time the food is to be taken. Above everything else, do not tell the patient to eat all he can and in addition take as much milk and as many eggs as possible. The amount of food should not be arbitrarily fixed, but should vary with each patient. If 3 qts. of milk and 6 eggs lead to a disordered digestion the amount should be kept just below the point which will cause such disturbances. The amount of forced feeding should depend on the extent of the disease and the amount of weight lost. Early cases with slight loss of weight, as a rule, will do well on three meals a day with very little forcing. Cases in which the disease is moderately or far advanced and in which there is great loss of weight should have the diet forced to a point compatible with good digestion.

Clapp<sup>1</sup> has recently contributed an article on this subject. He advocates three meals a day, at two of which meat is given, and in addition  $2\frac{1}{2}$  to 3 qts. of milk and 6 raw eggs. He gives the milk and eggs at breakfast and supper and at lunches (10 A.M., 4 and 9 P.M.).

My own preference is for one full meal in the middle of the day and the use of milk and eggs for the rest of the dietary. Four years' experience with this method of feeding has convinced me that it is capable of producing excellent results and is, in addition, very economical.

Arneill,<sup>2</sup> in writing on the digestive disturbances in pulmonary tuberculosis, states that the dangers of forced feeding are overemphasized. The two greatest dangers are bilious or auto-intoxication attacks and pathological obesity. The first is, I believe, the most frequent and most important. Bilious attacks are usually preceded by some anorexia, slight nausea, and a heavily furred tongue. Taken in time these attacks are usually very amenable to treatment. Reduction of the diet (particularly of the eggs), the use of saline purgatives, and a bitter tonic are usually efficient. Such attacks should not be neglected, as they are quite capable of leading to a fresh outbreak of the pulmonary symptoms.

In this connection I should like to call attention to the very instructive article by Edsall on the intolerance of fats. This article is reviewed by Dr. Steele in the present volume, p. 38.

As Arneill states, the average case of indigestion in the consumptive can be successfully treated along symptomatic lines. Bitter tonics, hydrochloric acid ferments, alkalies, and antifermentatives are used as

<sup>1</sup> Medical Record, June 29, 1907.

<sup>2</sup> Journal of the American Medical Association, July 6, 1907.

the symptoms indicate. Analysis of the gastric contents is rarely needed. Incipient cases differ very slightly from the normal, while the advanced cases usually have deficient hydrochloric acid and pepsin.

Last year considerable space was given to the subject of feeding in *typhoid fever*. It was then pointed out that, so far from getting the best results with the time-honored milk diet, patients were better nourished and less liable to complications if a more liberal policy was pursued.

F. T. Smith<sup>1</sup> is another advocate of more liberal diet. His experience is in accord with others who have adopted this plan of feeding typhoid fever patients, namely, that there is no greater tendency to the serious complications and, in addition, convalescence is shorter owing to the better nourished condition of the patients. He advises feeding typhoid patients on food they cared for, providing the food did not cause nausea or distention. Peabody and Gilman Thompson,<sup>2</sup> in discussing a paper by James, on The Management of the Intestinal Tract in Typhoid Fever, both advocated a more varied dietary in treating this disease. Peabody stated that for many years he had been in the habit of feeding patients solid food if they became hungry. He particularly recommends ice cream in all stages of the disease. Both speakers alluded to the value of *turpentine* both internally and externally in the treatment of *meteorism*. The drug may be given in 10-minim doses every three hours.

Einhorn,<sup>3</sup> in writing on the dietetic treatment of *diabetes mellitus*, states that while an absolute meat and fat diet is ideal because of the low sugar content it cannot be borne except for a short time. The experience of most clinicians show that it is best to allow diabetics a limited amount of carbohydrates. Seegen's diet list for diabetics, which Einhorn considers the best there is, is as follows:

**SOLIDS.** *Allowed in Any Quantity.* Meat of every kind: smoked meat, ham, tongue; fish of every kind: oysters, mussels, crabs, lobsters; meat jellies, aspic, eggs, caviar, cream, butter, cheese, and bacon. Of vegetables: spinach, lettuce, endive, Brussels sprouts, pickles, fresh asparagus, watercress, sorrell, artichokes, mushrooms, nuts.

*Allowed in Moderate Quantity.* Cauliflower, carrots, turnips, cabbage, green beans; berries, such as strawberries, raspberries, currants; also oranges and almonds.

*Forbidden Absolutely.* All foods made from flour or meal; bread is allowed in moderate quantities, according to the physician's orders; sweet potatoes, rice, tapioca, arrowroot, sago, grits, vegetables, green peas, cabbage; sweet fruits, especially grapes, cherries, peaches, apricots, plums, and dried fruit of every sort.

**BEVERAGES.** *Allowed in Any Quantity.* Water, soda-water, tea, and coffee. Of wines: Bordeaux, Rhine wine, Moselle, Austrian, and

<sup>1</sup> British Medical Journal, October 20, 1906.

<sup>2</sup> Medical Record, March 30, 1907.

<sup>3</sup> Journal of the American Medical Association, December 29, 1906.



Hungarian table wines—in a word, all wines that are not sweet and that do not contain more than the average amount of alcohol.

*Allowed in Moderate Quantity.* Milk, bitter beer, unsweetened almond milk, lemonade without sugar.

*Forbidden.* Champagne, sweet beer, cider, fruit wine, sweet lemonade, liqueurs, fruit juices, water ices, sorbets, cocoa, and chocolate.

Einhorn gives the following as an example of the dietary to be used:

	Calories.
Breakfast: Three eggs . . . . .	240
Half a roll (20 grams) . . . . .	50
Butter (30 grams) . . . . .	251
Coffee (150 grams), milk (100 grams), cream (50 grams)	203
Dinner: A plate of soup (200 grams), with egg . . . . .	85
Meat (200 grams) . . . . .	200
Half a roll and butter (15 grams) . . . . .	175
Asparagus with butter sauce (salad) . . . . .	30
Supper: Oysters or fish (100 grams) . . . . .	100
Three scrambled eggs with butter (15 grams) . . . . .	365
Half a roll with butter (15 grams) . . . . .	175
Westphalian ham (50 grams) . . . . .	200
Apples, tea, and cream (50 grams) . . . . .	138
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Two years ago<sup>1</sup> Gilman Thompson's views on the dietary for diabetics were given. The views he then expressed, favoring a more liberal diet in the feeding of diabetics, were concurred in by those discussing Einhorn's paper. It is now believed that in the end better results are obtained by allowing a moderate quantity of carbohydrates. Cutting the carbohydrates off entirely commonly results in the patient eating them any way.

Another factor which has led to a more liberal dietary is the knowledge that the appearance of acetone is more dangerous than the presence of sugar. The occurrence of acetone and diacetic acid is said to be prevented by the use of alkaline mineral waters. If diabetic coma develops bicarbonate of soda, added to normal salt solution to the point of saturation and given under the skin, is said to have been successful.

**Digitalis.** The necessity of being assured of a physiologically active preparation of a drug is of the greatest importance, and of no drug is this more true than of digitalis. Its frequent employment in grave and urgent cardiac troubles demands that the preparation used shall be efficient and certain in its action. While the importance of having an active sample of digitalis is fully recognized, there is as yet no method of accurately standardizing the various preparations so that we can always be certain of its effects. The reliability of the manufacturer and the

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1905, p. 331.

druggist seems to be our only safeguard at the present time. It has happened that samples of the tincture of digitalis obtained from a number of different sources have varied from absolute inefficiency to one capable of giving good results.

Furthermore the efficiency of digitalis seems to be dependent on certain details relating to the time the leaves are picked and their after-care. The leaves should be gathered at the time of the plant's blossoming and not in damp weather. They should be carefully dried, at not too high a temperature, and kept in a dry place. It has also been shown that the potency of the leaves seems to vary during the time of their development; those leaves gathered early in the summer are not nearly so effective as those gathered later in the summer.

Wang<sup>1</sup> has made a study of preparations made from leaves gathered over a number of years. He was able to confirm Focke's<sup>2</sup> contention that if good leaves are carefully dried and powdered and kept in dry and sealed jars they lost very little of their efficiency. When kept in the ordinary way and exposed to the air they rapidly deteriorate. As they are highly hygroscopic, enzymes that break down the glucosides act very readily on those exposed to air and moisture. Inasmuch as the tablet triturates of digitalis are extremely uncertain in their action, it is possible that this same enzyme reduction is responsible.

Löwy,<sup>3</sup> in a study of the infusion of digitalis, states that ready-made infusions should be rejected and only freshly made ones used. He states that an infusion which stands at room temperature for twenty-four hours loses much of its efficiency, due to presence of organic acid. The effects of this acid and of the hydrochloric acid in the stomach can be avoided to some extent by neutralization. In prescribing digitalis care should be taken to use only those preparations guaranteed by a reputable manufacturer as being physiologically efficient.

Of the preparations to be preferred are the tincture and the fluidextract, although Hatcher<sup>4</sup> believes that *digitoxin* bids fair to displace digitalis, as it more nearly represents the leaf. The objections to digitoxin are its insolubility in water, its irritant action, and the narrow margin between the maximum efficient dose and one which will produce a cumulative effect. The dose of digitoxin is from  $\frac{1}{250}$  to  $\frac{1}{4}$  grain. It is best given in a solution of glycerol-alcohol which consists of glycerin 333, distilled water 146, and alcohol (95 per cent.) 580 parts.

Edmunds<sup>5</sup> in a research on the influence of *digitalis*, *strophanthus*, and *adrenalin* on the velocity of the blood current, concludes that there is an acceleration of the blood stream followed by a retardation under

<sup>1</sup> Abstract, New York Medical Journal, December 29, 1906.

<sup>2</sup> Therapie der Gegenwart, 1902, p. 44.

<sup>3</sup> Wien. klin. Wochenschrift, 1907.

<sup>4</sup> Journal of the American Medical Association, December 22, 1906.

<sup>5</sup> American Journal of Physiology, February, 1907.

the influence of larger doses. He believes that this acceleration of the blood stream may account for the benefits derived from digitalis. The increased velocity of the blood current not only furnishes a better blood supply with improvement of nourishment, but also aids in the removal of waste products.

Hatcher<sup>1</sup> quotes Cushny and Sollmann to the effect that digitalis or digitoxin in therapeutic doses retards the velocity. It would seem, however, that the increased amount of blood thrown into the arteries and the associated rise in the arterial pressure would increase rather than retard the velocity of the current.

Hewlett<sup>2</sup> has reported an interesting instance of arrhythmia due to digitalis. While in bed in the hospital the patient's pulse varied between 82 and 90 per minute. Because of dyspnoea he was given digitalis. Ten days later the pulse fell rather suddenly to 46 to 60 per minute, and at the same time became irregular. The digitalis was stopped and four days later the pulse became normal. Two subsequent trials of digitalis produced the same effect. During this period of arrhythmia the patient complained of precordial distress. The dropping was apparently not due to extrasystoles, as during the intermissions there was absolute silence or at most a soft sound at the base (auricular contraction?). This is not the effect produced by the ordinary cumulative doses. The latter resemble the symptoms produced by digitalis poisoning and are characterized by a hobbling dirotic pulse and a tumultuous cardiac beat. The pulse may be slow and full when the patient is in the recumbent position, but becomes irregular when he sits up. According to Mackenzie digitalis produces a block between the auricle and ventricle only when the conduction of impulses across the auriculo-ventricular fibers is already impaired. Hewlett states that the subject has a distinct practical aspect, for if the interval is very short (0.2 of a second or less) digitalis is not responsible, while if it exceeds 0.2 of a second digitalis should be used carefully, as it is apt to produce a block at the auriculoventricular junction.

The use of digitalis in *aortic incompetence* is believed by many to be bad practice. This view is based on the fact that digitalis lengthens the diastole, thereby allowing of greater regurgitation of the blood; and, in addition, increases arterial tension, which is already abnormally high. Rankin<sup>3</sup> does not agree with this view. He states that digitalis is the best tonic to the myocardium that we possess. So long as compensation is maintained digitalis is never indicated, but whenever this fails it should be used, irrespective of the character of the valvular lesion.

For cases of ruptured compensation due to aortic disease, Rankin gives 15 minims of the tincture of digitalis every four hours. The drug

<sup>1</sup> Loc. cit.

<sup>2</sup> Journal of the American Medical Association, January 5, 1907.

<sup>3</sup> British Medical Journal, March 16, 1907.

is withdrawn or reduced to 10 minims every eight hours when the cardiac rhythm becomes very slow, the urinary output is diminished, and there is disturbance of the digestive organs. Rankin also calls attention to the fact that combining nitroglycerin with the digitalis renders the use of digitalis safer in aortic disease by preventing an increase in the arterial tension.

Last year Bruce<sup>1</sup> expressed much the same views on digitalis and aortic incompetence. In commenting on Bruce's views, it was advised that these cases, as a rule, are better treated with strophanthus or sparteine, but, if they fail, digitalis may be tried.

In the treatment of *scarlatinal nephritis* associated with a weak pulse Cotton<sup>2</sup> recommends the following:

R—Potassii acetatis,  
Potassii citratis . . . . . ʒʒ gr. xcvj  
Infusi digitalis . . . . . q. s. ad fʒiij.—M.

Sig.—A teaspoonful every four hours to a child from five to ten years of age. Follow each dose with half a tumblerful of water.

**Electricity.** For many years the employment of electricity in general medicine was viewed somewhat skeptically by the profession, largely due, no doubt, to its having fallen into the hands of charlatans. With the discovery of the *x*-rays by Röntgen, however, other forms of electricity have been more generally employed. Shoemaker,<sup>3</sup> in a review of the uses to which electricity may be put, cautions against looking upon it as a cureall. It should be regarded simply as an adjuvant to other treatment.

A form of electricity which has been attracting considerable attention during the past few years is that known as the *high-frequency currents* advocated by d'Arsonval.

The high-frequency or high-potential currents are characterized by an extremely rapid rate of oscillations said to be 1,000,000 per second and by a voltage approaching 1,000,000; the amperage, however, is very low. They are composed of the Morton wave currents, obtained from the static machine; the Tesla currents, obtained by means of primary and secondary coils, and the d'Arsonval currents, obtained from the solenoid or the Oudin resonator. D'Arsonval has shown that these high-frequency currents are not injurious to the human body, nor are they painful, but produce a sensation of warmth. His experiments indicate that the currents have a decided influence on metabolism and cell production. According to the observations of d'Arsonval and others, respiratory combustion and carbonic acid elimination are increased, the output of urea is greater, and there is increased diuresis and a better elimination of excreta. The process of nutrition is both stimulated

<sup>1</sup> PROGRESSIVE MEDICINE, December, 1906, p. 305.

<sup>2</sup> Journal of the American Medical Association, March 9, 1907, p. 900.

<sup>3</sup> Pennsylvania Medical Journal, 1906.

and regulated and the capacity for work better. The hemoglobin is also said to be increased.

Pfahler<sup>1</sup> reports good results from the use of the high-frequency currents in *chronic rheumatism* and *rheumatoid arthritis*. Pfahler believes that the currents produce several effects, all of which tend to favorably influence both local and general metabolism. Constitutionally the passage of the currents through the body usually raises arterial pressure and increases tissue change. Locally a favorable effect is obtained by the passage of the electricity, the counter-irritation which is produced by the multiple sparks from the glass electrode, and to some extent from the violet rays and the slight amount of *x-rays*. Pfahler reports one case of rheumatoid arthritis in detail in which joint function was greatly improved and the patient, after being completely incapacitated, was able to return to her work. I have seen a case of rheumatoid arthritis markedly benefited by the high-frequency currents. Borshinger<sup>2</sup> has used the high-frequency currents in four cases of *tuberculosis* in an advanced stage. In one the result was excellent.

Thillé,<sup>3</sup> who has had a large experience with the high-frequency currents, has published a monograph giving the results obtained in 26 cases of tuberculosis. All of the cases treated belonged to the laboring class; 14 were cured and 9 of them were doing hard manual labor; 1 patient, although greatly improved, refused further treatment; 4 patients, still under treatment, were greatly improved; 7 were not cured, but the treatment of these 7 was undertaken as an experiment. None of the patients received any drugs while under treatment.

According to Thillé, in addition to causing a disappearance of the symptoms (cough, expectoration, dyspnea, etc.), there was also a marked improvement in the general condition of the patients treated. While the current is generally credited with the power of increasing the general nutrition, it must be borne in mind that the psychic effect of such treatment in tuberculous individuals must not be overlooked as a factor in their improvement.

The use of electricity in the various manifestations of *cardiovascular disease* has not received much attention. D'Arsonval has stated, from animal experimentation, that the high-frequency currents tend to produce a lowering of blood pressure and that even normal pressure may be reduced. Clinically this has been confirmed by Hautier, who has used the currents in arteriosclerosis for the purpose of diminishing the hypertension. Galli<sup>4</sup> asserts that a general application of the high-frequency current reduces while the local application elevates blood pressure. Pfahler<sup>5</sup> also states that the constitutional effect of the current is to produce an increase in the arterial tension.

<sup>1</sup> Pennsylvania Medical Journal, 1906.

<sup>2</sup> Ibid.

<sup>3</sup> Editorial, New York Medical Journal, July 20, 1907, p. 126.

<sup>4</sup> Gazzetta degli Ospedali, 1906, No. 153.

<sup>5</sup> Loc. cit.

Galli uses the galvanic current in the form of local or general baths in the treatment of cardiac cases. The effect produced is similar to that seen after the use of carbonic acid baths; in some cases the electric baths may be substituted for the carbonic acid baths.

In anemic, nervous individuals, suffering from arteriosclerosis and renal symptoms, faradic baths seem preferable. He has also found that the high-frequency current exerts a favorable action on the physical and psychical depressions which sometimes occur in the course of chronic heart disease.

**Exercise.** Hygiene in its broadest sense is receiving more and more attention from physicians. Attention to diet, plenty of fresh air, and regulation of exercise are no longer distinctive of the treatment of tuberculosis. Every year sees the application of hygiene in the treatment of disease more widely applied. At present the application and the limitations of exercise are less understood than the questions of feeding or fresh air, and the suggestion of Storey<sup>1</sup> that physical instruction shall become more generally adopted in all teaching institutions is an excellent one.

The use of *pulmonary gymnastics* in the treatment of *pulmonary tuberculosis* has been commented on in these pages in previous years. Minor<sup>2</sup> has contributed an article on this subject much of which I cannot endorse. That such exercises are of benefit as a prophylactic measure there can be no doubt. Much can be accomplished with chest gymnastics in children with a bad hereditary history or where for other reasons a maximum lung capacity is called for. Such exercises are also of the greatest benefit in those with badly shaped chests or in those recovering from pneumonia or pleurisy, in order to restore the functional capacity of the lung.

It is quite possible that too strict adherence to rest may be harmful to the tuberculous patient and that later we may find that a greater degree of latitude will be advisable. It seems quite certain, however, that the number of people injured by rest is very small, while there is almost daily evidence of the fact that harm has been done by means of exercise of one sort or another. In regard to the use of pulmonary gymnastics in pulmonary tuberculosis, I would most positively take sides with those who advise rest, so far as possible, for the affected lung. The ultimate object in dealing with a tuberculous focus in a lung is to obtain the transformation of the diseased tissue into fibrous or scar tissue. It is perfectly evident that this takes time, particularly in an organ subject to constant motion. I cannot conceive the advantage of subjecting delicate fibrous bands, which are just forming, to the strain of increased expansion, with the possibility of extending the diseased process. There is no doubt that most cases, as a result of the changed conditions under

<sup>1</sup> Journal of the American Medical Association, July 20, 1907.

<sup>2</sup> Therapeutic Gazette, October, 1907.

which they live in being treated for tuberculosis, have some increase in the chest expansion. This I believe is entirely sufficient and need scarcely ever be augmented by pulmonary gymnastics.

For those who are tempted to prescribe pulmonary gymnastics in a tuberculous individual it must be remembered that they should never be used when there is a subnormal temperature, a fever of 100° F. or more, in cavity formation, in acute exacerbations of the disease, in the presence of a rapid pulse, marked dyspnea on exertion, marked loss of weight, blood spitting, recent pleurisy, or any complication. These same restrictions apply to any form of exercise.

The question of the effects of excessive exercise on the various vital functions is not yet satisfactorily settled. My own belief is that excessive exercises such as football, rowing, running, etc., are not of themselves so injurious as some have claimed. This at any rate applies to pulmonary disease. The trouble arises largely because so many men abruptly change their method of living after leaving college. From a healthy, active out-of-door life they suddenly change to sedentary life in closed, illy ventilated rooms.

So far as changes in the heart, bloodvessels, and kidneys are concerned the explanation is not so simple. As has been pointed out,<sup>1</sup> the observations so far made on the cardiovascular changes in athletes are lacking in value, in that they do not extend over a sufficiently long period of time.

**Fresh Air.** It is a curious fact that nearly every innovation in medicine has had its prototype in some long-forgotten observation the value of which has escaped notice. Thus it was pointed out in last year's review that Benjamin Franklin had observed that "common colds" were not due to exposure, but were transferred from one infected individual to another. Franklin specifically pointed out that those who led an out-door life and were exposed to all the inclemencies of the weather were less subject to "colds" than those living in badly ventilated houses or who expose themselves in overcrowded assemblage places. Gilman Thompson<sup>2</sup> also quotes observations of Austin Flint and John H. Griscom, made over fifty years ago, in which it was noted that typhus-fever patients seemed to do better when treated out of doors in tents than those treated in hospital wards. In both these instances overcrowding and lack of facilities rendered this method of treatment necessary and not the one of choice. These observations gain additional interest now that we are experiencing a revolution in favor of fresh air. The climatic treatment (really fresh-air treatment) was first systematically applied in a single disease—tuberculosis. The efforts of Bremer and Detweiler in Germany and of Trudeau in this country met with scanty recognition for years. The universal recognition of the value of fresh air in dealing

<sup>1</sup> Journal of the American Medical Association, October 27, 1906.

<sup>2</sup> Medical Record, February 9, 1907.

with tuberculous diseases is now so widely accepted that one is apt to forget that it is practically only within the past ten or fifteen years that this principle has been generally adopted.

Within the past few years the fresh-air treatment of *pneumonia* has gained a considerable following, largely due to the efforts of Northrup, of New York. The inhalation of pure oxygen was believed at one time to be very useful in pneumonia, but of late years one hears less of its employment, the consensus of opinion being that it is of doubtful value. Northrup's claim for fresh air in the management of pneumonia is undoubtedly a rational one, as it is certainly a more common-sense way of furnishing the oxygen. The only criticism on Northrup's claims that can be made is his insistence on cold air. To state that the air must be cold is, I believe, as erroneous as to assert that tuberculosis, for instance, can only be cured in this or that climate. The essential principle in both is that the air be fresh. To state that pneumonia must be treated by cold air or tuberculosis in some specific climate robs both measures of their value for the reason that cold air cannot always be obtained in the case of pneumonia and climatic requirements are unobtainable for the majority of tuberculous cases. The fact that constant exposure to fresh air tends to increase the number of red blood cells, improve nutrition, and allay nervous symptoms, has recently led to its adoption in the management of other conditions such as *septicemia*, *pernicious anemia*, and *typhoid fever*. In fact there is no diseased condition that can be made worse by having a liberal supply of fresh air. The only exception to this is that *cold* fresh air is not well borne by individuals with kidney lesions or by those with marked debility and a feeble circulation such as are met with in some cases of advanced tuberculosis.

Gilman Thompson<sup>1</sup> has contributed a very interesting article on the question of fresh air in *hospital wards*. He points out what becomes patent to all of us if we stop to consider, namely, that the present method of ventilating wards is entirely inefficient. Either the windows are open but for a short time each day, or, what is more frequently the case, superheated air is forced into the ward through thousands of feet of metal conduits. In the latter instance the air is never fresh, but "cooked" and largely robbed of its invigorating principles before it reaches the ward.

The recognition is being forced upon us that if one cannot maintain health in illy ventilated rooms it is increasingly difficult to restore health under such conditions.

Thompson states that some years ago while simultaneously visiting in two hospitals he had occasion to note that certain classes of patients, especially those with marked anemias, chronic sepsis, pulmonary and chronic cardiac diseases, did much better in one institution than in the other. One hospital was modern and up to date, receiving its air in a

<sup>1</sup> Loc. cit.



superheated condition, through metal conduits. The other was old, the windows had become settled, and gusts of air constantly blew in. The wards were heated by steam pipes, and when too hot or close the windows were left open, sometimes all day. The difference was so strikingly in favor of the older institution that patients were later placed out of doors on the balconies.

The night temperature of a general hospital ward should be 5° F. below the noon-day temperature, which latter should not be above 68° or 70° F.

Northrup<sup>1</sup> has coined the term "the twenty-three-hour treatment." This treatment consists in living twenty-three hours of the twenty-four in the best obtainable cool, flowing, fresh air. It is especially beneficial in the convalescence of acute illnesses, in cases of delicate children, or those not thriving properly. Northrup calls attention to the fact that cold air may be stale while warm air may be thoroughly oxygenated and free from odors. Cool air is more soothing and beneficial, but the essential point is that, whether warm or cool, the air should be kept in motion.

Burt<sup>2</sup> is an advocate of treating *pneumonia* by means of plenty of fresh air. He deprecates the use of drugs, especially alcohol and opium. Barr<sup>3</sup> also advocates liberal ventilation for the pneumonia patient. The room temperature should be maintained between 60° and 65° F. He emphasizes the fact that the administration of oxygen in cases where the sick-room is illy ventilated is not only unscientific but absurd. He also condemns the use of the bronchitis kettle in treating pneumonia, asserting that it has been responsible for many deaths. Thompson<sup>4</sup> states that in 1906 there were treated at the Presbyterian Hospital, New York, 128 cases of pneumonia. Of these patients 47, or 36.7 per cent., received absolutely no drugs whatever aside from an occasional laxative. All of these 47 cases made a complete recovery in the usual time without any medication, and for the most part lying close to open windows in mid-winter weather.

I do not think there can be any doubt but that the liberal supply of fresh air for pneumonia patients and others is an innovation that has come to stay. I do not think it is wise, however, for anyone to get the impression that the mere placing of a pneumonia patient in the open air is all the treatment required. While it is no doubt true that this method will greatly reduce the necessity for meeting symptoms, there will always be, I believe, a certain number of cases in which the physician will need to exercise his skill to avert a fatal outcome.

Markoe<sup>5</sup> and Stone<sup>6</sup> have pointed out the advantage of the open-air treatment in dealing with some of the *complications of pregnancy* and the

<sup>1</sup> Archives of Pediatrics, April, 1907.

<sup>2</sup> Medical Record, March 30, 1907.

<sup>3</sup> Medical Press and Circular, April 24, 1907.

<sup>4</sup> Loc. cit.

<sup>5</sup> Bulletin of the Lying-in Hospital, September, 1906.

<sup>6</sup> Medical Record, February 9, 1907, p. 246.

puerperal state. Women suffering from the puerperal septicemias are greatly benefited by fresh air. Pale, anemic women from the tenements are also greatly improved by a sojourn on the roof of the hospital while waiting to be confined.

Mabon<sup>1</sup> states that the experience of the Manhattan State Hospital for the past five years shows conclusively that the open-air treatment is particularly beneficial for the following classes of the *insane*: (1) The tuberculous; (2) the feeble and untidy; (3) the retarded convalescents, and (4) the acute insane, in whom the psychosis is associated with anemic blood states, delirium, and loss of sleep.

James<sup>2</sup> has found the use of fresh air most useful in a variety of conditions, both acute and chronic. He has noted particularly good results in *puerperal fever*, *typhoid fever*, in which to a certain extent it had taken the place of cold baths, and *cerebrospinal meningitis*, in which it had an excellent effect on the nervous symptoms. The consensus of opinion expressed in the discussion of James' paper was that most diseases could be greatly benefited by better ventilation.

A very instructive article on the *home treatment of tuberculosis* has been contributed by Donald.<sup>3</sup> He points out what is too little appreciated, namely, that about 98 per cent. of the cases of tuberculosis must be treated at home and usually by the family physician. Furthermore, many of these individuals must support themselves as well as aid in supporting others while they are under treatment. Donald emphasizes, what has been repeatedly stated in these reviews, that the treatment of tuberculosis is largely the treatment of malnutrition. A poor climate with good food and cheerful surroundings is infinitely superior to the best climate possible with poor food and cheerless surroundings.

Another important point which Donald emphasizes is the necessity of recognizing the disease in its early stages, for at this period tuberculosis is very amenable to treatment; taken late it too often is a hopeless task to do anything more than slightly prolong life.

Donald's conclusions give an excellent summary of his experience:

1. All cases under observation have received little treatment except rest, fresh air, and forced feeding.
2. Internal medication has been used wherever necessary, usually to meet symptoms and to cure any aberration from the normal plane of health, at the earliest possible moment.
3. All cases have been relieved of the evening rise of temperature.
4. All have gained in flesh—the maximum gain being twenty-four pounds, and the minimum five.
5. All patients have been able to resume their ordinary avocations, and have been able to support themselves, and in some cases aid in supporting others.

<sup>1</sup> New York Medical Journal, February 9, 1907.

<sup>2</sup> Medical Record, December 8, 1906, p. 926.

<sup>3</sup> Therapeutic Gazette, September, 1907.

6. The lung lesions have shown no striking improvement on physical exploration, but the general sense of well-being in all cases has been marked.

7. All these patients understand the condition of their lungs perfectly, all are hopeful of a cure, and all are filled with the belief that they will be cured, a belief which I, by the way, have carefully fostered.

8. All of these patients, understanding the condition of the lungs and being educated for the care of their sputum and excretions generally, are centres for a dissemination of knowledge of this white plague.

9. Only by a widespread dissemination of this knowledge can we ever hope to stamp out the scourge; and only by careful instruction of our patients can we hope to eliminate them as potent factors for evil through the medium of their sputum.

10. None of these cases have been cured in the year, but all have been checked, and all have been improved.

Martin,<sup>1</sup> of Lynn, Massachusetts, has also published a paper giving his experience with the *home treatment of tuberculosis*. He states that most of his cases have been from people of the poorest classes living under unfavorable conditions. The results obtained were remarkably good. Between the years 1898 and January 1, 1906, he had 197 tuberculous cases, all treated in their homes; 30 per cent. were "arrested," 49 per cent. were improved, and about 21 per cent. were not improved.

An article by Bowditch and Griffin,<sup>2</sup> giving the subsequent histories of cases of *tuberculosis* treated at the Sharon Sanatorium, is of interest. This institution, situated just outside of Boston, was started by Dr. Bowditch, in 1891, for the purpose of caring for working women. An especial interest is attached to this report because the Sharon Sanatorium has none of the so-called climatic advantages. Since the opening of the institution in February, 1891, up to January, 1906, there were discharged 362 patients. Of this number 35 either remained too short a time or proved to be non-tuberculous, leaving 327 to be considered. Bowditch prefers the term "arrested" to "apparently cured" in classifying patients who have been relieved of their symptoms. A study of the ultimate results obtained in cases discharged from the institution as arrested gave the following:

*From the Year 1891 to 1906.*

Total number "arrested" . . . . .	160
Number still living and well, most of them housekeepers or wage-earners . . . . .	134 (83 + p. c.)
Number who have not recently been heard of, but who at last accounts were doing well, many of them in robust health . . . . .	5 ( 3 + p. c.)
Number who have since relapsed and died . . . . .	21 (13 + p. c.)

<sup>1</sup> American Medicine, February, 1907.

<sup>2</sup> Journal of the American Medical Association, June 15, 1907.

These results are sufficiently encouraging to warrant the adoption of similar institutions wherever possible. Another encouraging feature of the work of such sanatoria is their educational effect. In regard to the relative merits of the so-called "home" and "climatic" treatment Bowditch has the following to say:

"We know now that an immense deal of good has been and still can be accomplished by the methods which are being adopted more and more near the homes of patients suffering from tuberculosis. It has been satisfactorily proved that much more has been done in these ways than was thought possible fifteen years or even a decade ago. I cannot sympathize, however, with what I feel to be the extreme views of some observers who, because of the success of these less radical measures in a large number of cases, maintain the opinion that there is not the slightest use in ever sending a phthisical patient away from home to a distant climate. Such an opinion is inconsistent with my own experience in certain patients whom I have seen improve by such a change after a discouraging attempt to improve near home."

This is I believe a conservative and fair estimate of this much discussed question. The only criticism to be made on it is that it does not sufficiently emphasize that climatic treatment is beyond the means of the great majority of tuberculous patients. It has been my experience that the choice between home treatment and treatment at some one of the climatic resorts rests ultimately on the question of money.

In arriving at a decision in any particular case the following facts should be kept in mind. (1) Do not advise a patient to go away without ascertaining his financial condition. To tell a patient that his only hope lies in getting away is utterly valueless if he has not the means. Too often patients with little or no money avail themselves of such advice, only to become a burden to the particular community in which they settle. (2) Do not advise hopelessly diseased patients to try the advantages of climate, even when expense need not be considered. (3) Do not send a patient to a place out of reach of a physician familiar with the management of tuberculous cases. The admonition "to go west and rough it" has been the undoing of many a patient who should and would have probably recovered had his daily life been properly supervised. If home treatment has accomplished nothing else it has taught us that attention to the details of each individual case is quite as important as anything else.

Knight<sup>1</sup> has called attention to the importance of the after-treatment of apparently cured cases of tuberculosis. The better class of patients usually appreciate the importance of reporting to their physician at regular intervals and of continuing a hygienic mode of life. The poorer class of patients, however, usually drop out of sight after they have been

<sup>1</sup> Journal of the American Medical Association, July 27, 1907

relieved of their symptoms. Every effort should be made to prevent these cases from returning to an infected house or shop. And they should be thoroughly instructed in the danger of not continuing a hygienic life for years after leaving the sanatorium. Convalescent farms are urgently needed in connection with sanatoria devoted to the working class.

Sabatucci<sup>1</sup> has had such excellent results in the treatment of *surgical tuberculosis* at a sea-side sanatorium that he has largely abandoned early operations in such cases. Non-operative interference in dealing with surgical tuberculosis is destined, I believe, to become more generally adopted.

Carling<sup>2</sup> expresses a preference for inland rather than sea-side resorts in treating surgical tuberculosis. The ideal location in his opinion is one situated at a moderate altitude away from the sea-shore. He gives as his reasons: (1) The air is more invigorating; (2) the absence of damp and fog; (3) more days of sunshine; (4) better natural drainage; (5) a firmer soil for locomotion.

Until quite recently surgical tuberculosis was thought to be especially benefited by a sojourn at the sea-side. This was largely due to the fact that the French Sanatoria devoted to the treatment of surgical tuberculosis were all so situated. There is no doubt but what surgical conditions are greatly benefited at the sea-side, but that the air at such resorts is in any way specific is doubtful. The good results obtained have probably been due more to the constant outdoor life than anything else.

Oppenheimer<sup>3</sup> advocates the use of solar baths in the treatment of *tuberculous peritonitis*. He reports two cases in which the rays of the sun were allowed to shine for definite periods directly on the abdomen, while the children were out of doors. His theory is that the sun's rays produce a local hyperemia of the peritoneum similar to that brought about by a laparotomy. The efficiency of such treatment can only be determined by seeing what results can be obtained by the ordinary outdoor life such as is employed so successfully in other manifestations of tuberculosis.

Lack of space forbids any detailed account of Woodruff's<sup>4</sup> observations on the *physiological action of light*. It may be stated, however, that he has amassed a great many facts, experimental and otherwise, to show that continual exposure to sunlight may result in an excess of stimulation which may prove harmful. This is of interest because it has for years been taught that the ideal climate for tuberculosis is the one with a maximum number of clear days and every report on the subject lays the

<sup>1</sup> *Gazetta Medica di Roma*, December 1 and 15, 1906.

<sup>2</sup> *New York Medical Journal*, June 8, 1907.

<sup>3</sup> *Zeitschrift f. physikalische und diätetische Therapie*, January, 1907

<sup>4</sup> *American Medicine*, April, 1907.

greatest stress on this point. It is apparent that the whole subject of the action of light in unlimited quantities is not settled and that additional observations are needed.

**Hyoscine or Scopolamine.** Birchmore<sup>1</sup> has contributed a paper on "Hyoscine Sleep in Obstetric Practice." He administers hypodermically hyoscine gr.  $\frac{1}{100}$ , morphine gr.  $\frac{1}{4}$ , and cactine gr.  $\frac{1}{8}$ . The first dose is given as soon as the first stage of labor has certainly begun. This is usually sufficient until the expulsive pains are pronounced. As soon as the patient shows the least evidence of perception a second dose is given. When instrumental aid is necessary a third dose may occasionally be given. Birchmore states that in his experience there were no untoward effects either in the mother or child and that the length of the labor was usually shorter than under ordinary conditions.

With the exception of the addition of cactine this method differs in no way from Schneiderlein's scopolamine-morphine anesthesia. During the past year a large number of cases have been reported from the German clinics on the use of scopolamine-morphine anesthesia in obstetrical work. In the discussion following the reading of several papers before the Obstetrical Society of Berlin<sup>2</sup> it was the general opinion that this method was not without danger, and was not to be commended for the use of the general practitioner. It is capable of producing marked untoward effects. A number of deaths have been reported after its use; many of the children have been born asphyxiated; labor pains have been interfered with, and the placenta came away more slowly than is ordinarily the case. This method of anesthesia should never be used in private houses; with the greatest precautions it may be employed in hospitals, where patients are under constant supervision.

Steffen's<sup>3</sup> opinion of the method is in agreement with that just expressed. From an extended review of the method he concludes that: (1) The method does not accomplish the desired results. (2) It cannot be regarded as harmless for mother and child. (3) It is not to be recommended for use in private practice, as the by-effects which are liable to develop make it necessary that medical aid can be summoned at any moment.

Van Meter<sup>4</sup> reports a death following the hyoscine-morphine-cactine anesthesia. The patient left the operating table in good condition, but died suddenly a few hours later from respiratory failure.

The addition of cactine to the mixture, as recommended by Birchmore, is a useless precaution, as it has been shown by Hatcher (see *Cactus grandiflorus*) that this so-called active principle of *Cactus grandiflorus* is absolutely inert and incapable of producing any effect.

<sup>1</sup> Medical Record, January 12, 1907.

<sup>2</sup> PROGRESSIVE MEDICINE, September, 1907, p. 188.

<sup>3</sup> Archiv f. Gynäkologie, lxxxi, Nr. 2.

<sup>4</sup> Journal of the American Medical Association, August 3, 1907.

**Iodide of Calcium.** A. G. Peter<sup>1</sup> reports favorably on the use of calcium iodide in the treatment of indolent and sluggish *leg ulcers*. Under the use of the drug the ulcers healed up and the indurated tissue about them either was greatly diminished or entirely disappeared. Peter also found this salt of benefit in the treatment of *syphilitic necrosis* of the nasal bones and in the headaches associated with syphilis.

The drug is given in doses of from 2 to 4 grains three times daily. The dose recommended by Peter is 2 grains. Aqua menthæ piperitæ is an excellent vehicle in which to administer the drug.

**Iodide of Potassium.** Burnet<sup>2</sup> believes that in chronic diseases of the respiratory tract iodide of potassium is most valuable. In the pulmonary fibrosis as met with in stone-masons he found that iodide of potassium and *ichthyol* were the only two drugs capable of producing favorable results. The dyspnea, which is so frequent in these cases, is very favorably influenced by a prolonged course of the iodides.

If one can be absolutely certain that a pulmonary lesion is not due to tuberculosis, the use of the iodides may be permitted. While at the present time there is considerable difference of opinion as to the danger of iodide of potassium in pulmonary tuberculosis, I am personally convinced that the use of the drug is unsafe.

Several years ago I attempted to obtain some experimental evidence on the subject, but the results obtained were not conclusive one way or the other. During the past year, however, I<sup>3</sup> have had a very conclusive clinical demonstration of the fact that the administration of iodide of potassium to a tuberculous case is a dangerous procedure. In this instance a woman with a suspected apical lesion was given iodide of potassium in 5-grain doses every three hours in order to obtain some sputum. The woman had no symptoms of tuberculosis and the signs at the right apex were indefinite. On the third day her temperature rose abruptly, cough developed, and an abundant expectoration containing tubercle bacilli was obtained. Fever of a hectic type continued up to the time she left the hospital, three weeks later.

The diagnostic use of iodide of potassium in cases of suspected tuberculosis was introduced by Sticker and is advocated by Turban. There can be no doubt, however, that it is capable of arousing a latent lesion into undue activity. Greater familiarity with the early physical signs and symptoms of tuberculosis will render such aids unnecessary. If a diagnostic aid is needed, tuberculin had better be used.

Burnet<sup>4</sup> refers to the value of the iodides in the treatment of *angina pectoris*. To be of value the drug should be given in the quantity of from 30 to 60 grains a day and kept up for months. The value of the iodides in the management of arteriosclerosis and its various manifestations was alluded to in last year's review.

<sup>1</sup> British Medical Journal, April 27, 1907.

<sup>2</sup> Lancet, September 8, 1906.

<sup>3</sup> Therapeutic Gazette, April, 1907.

<sup>4</sup> Loc. cit.

Knox<sup>1</sup> reports a case of *actinomycosis* of the cheek cured by iodide of potassium. The drug should be given in the early stages of the disease. While advanced stages of actinomycosis may be benefited by iodide of potassium, the possibility of a cure is remote.

Guthrod<sup>2</sup> advocates the use of iodide for the prevention of *eclampsia*. He also uses the drug after abortion or where a macerated fetus has been born. Guthrod believes that the iodide has a direct action on the poison causing eclampsia and in addition promotes elimination by increasing the secretion of urine and strengthening the heart.

Iodide of potassium might be used as an aid in dealing with eclampsia, but a review of the enormous amount of work which has been done on eclampsia and other forms of toxemia in pregnancy indicates that no single drug will be of benefit. Pregnant women should be carefully watched and at the first indication of faulty elimination active measures must be instituted to stimulate the emunctories. For an excellent review of the whole subject of toxemia in pregnancy see Davis' article in the September number of *PROGRESSIVE MEDICINE*, 1907.

Iodine has recently been strongly advocated as an efficient antiseptic. Reference has been made in previous numbers of *PROGRESSIVE MEDICINE* to its use in gynecological conditions (Pryor) and to its use in general surgery, both as a hand disinfectant and in the treatment of infected wounds.

Cannaday<sup>3</sup> has written a review of the various uses iodine has been put to in surgery. He believes that it is the most perfect antiseptic we at present possess. According to Kinnaman, iodine in solutions ranging from 0.2 to 1.6 per cent. is more potent as a germicide than mercuric chloride, and far less toxic. Cannaday employs the following plan for hand disinfection: Thorough scrubbing of the hands with green soap and hot running water, taking special pains with nail folds, subungual spaces, and skin between the fingers. The nails are cleaned and the hands again scrubbed. The residue of soap is removed from the hands with 70 per cent. alcohol and the hands are then immersed for five minutes in a one-half of 1 per cent. alcoholic solution of iodine. The same solution is used to disinfect the operation site. The yellow stain may be removed from the hands with dilute ammonia water.

In the treatment of *arteriosclerosis* Senator<sup>4</sup> advises strict regulation of the diet. Meats should be reduced to a minimum. The so-called lactovegetarian diet is to be recommended in these cases. This diet consists of milk to which is added all kinds of carbohydrates, such as bread, farinaceous foods, gruels, fat, and green vegetables. Eggs may be allowed in small quantity. Fresh fish is allowable, but meat should not be taken at all or only in small quantities.

<sup>1</sup> *Lancet*, November 3, 1906.

<sup>2</sup> *Monatsschrift f. Geb. und Gynäk.*, xxiv, Nr. 5.

<sup>3</sup> *American Medicine*, November, 1906.

<sup>4</sup> *Folia Therapeutica*, April, 1907.



Oliver<sup>1</sup> also advises attention to the dietary in treating arteriosclerosis. He thinks that the bulk of each meal should be reduced. In regard to meat this should be reduced and, when given, should be boiled and served without the broth. The *iodine* preparations are very useful in the treatment of arteriosclerosis, and their good effect may be rendered still more marked by combining them with amyl nitrite or one of the other nitrites. Senator recommends the following formula:

R—Tinct. iodi . . . . . ℥xv  
 Spt. ætheris nitrosi . . . . . f5j—M.  
 Sig.—Twenty to thirty drops to be taken three or four times a day.

Perez<sup>2</sup> recommends iodine internally in the treatment of *typhoid fever*. He administers the tincture (B. P.) in doses of 3 to 15 minims diluted in 1 to 2 drams of rum or cognac and 1 to 2 ounces of water, to which a little sugar has been added. The iodine mixture is given three or four times daily. D. Walsh<sup>3</sup> gives the following directions for using iodine in typhoid fever: 2 minims of tincture of iodine and 1 minim of pure *phenol* are put in a tumbler of water. The patient is allowed to drink freely of this mixture during the day or night. Both writers state that the iodine seems to have a distinct influence in favorably modifying the symptoms. The tongue becomes clean, the diarrhea ceases, and the temperature is reduced.

**Iron.** A much-debated question, and one that has led to an extensive literature, is that relating to the respective merits of inorganic and organic preparations of iron.

In favor of the inorganic salts we have the testimony of experienced clinicians the world over that these compounds have an almost specific effect in increasing the amount of hemoglobin in chlorotic patients. The familiar results obtained with Bland's pill need only be mentioned. This familiar clinical fact, however, was not accepted by physiological chemists, who asserted that the animal organism was unable to synthesize complex substances from simple ones and, therefore, it was impossible for iron in simple inorganic form to be converted into hemoglobin. As additional support to this claim it was pointed out that the chick in developing from the egg obtained its hemoglobin from complex protein-iron compounds; that the iron obtained by suckling mammals is of a similar complex nature, and that iron obtained, under natural conditions, from the food is entirely of a complex nature. Finally it was asserted that as all the inorganic iron administered could be recovered from the feces there could be no benefit in giving it, as there was no absorption. Notwithstanding the vigor with which the many organic preparations have been pushed commercially, the older inorganic preparations have never been entirely supplanted.

<sup>1</sup> Lancet, May 18, 1907.

<sup>2</sup> British Medical Journal, July 20, 1907.

<sup>3</sup> Ibid., August 3, 1907.

Meltzer<sup>1</sup> is of the opinion that the clinical position in regard to iron has finally won the day and that the struggle over the relative merits of the two preparations is ended. Meyer,<sup>2</sup> who has collected and analyzed the evidence for and against the inorganic preparations, is also of the opinion that there can be no doubt that inorganic iron can be absorbed from the intestine and utilized in the formation of hemoglobin, when given in the usual medicinal doses.

For instance, it has been shown that the organs of animals that have been fed inorganic iron preparations regularly contain more iron than the organs of control animals. The liver is the great storehouse for iron just as it is for glycogen. Both are stored up in excess of the requirements of the organism. It is the opinion of both Meltzer and Meyer that no matter how the iron is combined when it enters the stomach, it is not used directly for the formation of hemoglobin, but is always first converted into the ferratin of the liver, which constitutes an intermediate step in the conversion of food iron into hemoglobin. This ensures a constant material for the formation of hemoglobin irrespective of the sort of iron compound obtained by an animal in its food.

It is believed that, no matter how much iron is administered daily, the amount absorbed is something less than 1 grain. In spite of this, however, the best results with Blaud's pill, in the treatment of chlorosis, are obtained by giving many times the amount of iron required. Chlorotic patients should have an abundance of fresh air in addition to the iron. The eliminative organs should also be kept active because of the constipating effect of the iron and also because the anemias are considered by many to be primarily toxic in origin.

**Morphine.** Stockman<sup>3</sup> calls attention to the value of morphine in lessening the spasm of involuntary muscles. For this purpose he has found it particularly valuable in *tenesmus* from any cause, in *renal* and *hepatic colic*, *severe vomiting*, *spasm of the cervix uteri*, *irritation of the bladder*, etc. It is well known that the severe colic and obstinate constipation of *lead poisoning* are frequently relieved by morphine. In these cases the drug relieves the spasm of the muscular coat of the bowel and thus allows purgatives to act.

Pulmonary dyspnea, associated with much consolidation of the lung, as in pneumonia, or excessive secretion, should not be treated with morphine owing to its depressing effect on the respiratory centre. Cardiac dyspnea is frequently benefited by morphine. Stockman states that in *bronchial asthma* nothing gives so much relief as a hypodermic of morphine. Recently he has had even better results in these cases by combining with  $\frac{1}{12}$  or  $\frac{1}{8}$  of a grain of morphine 5 to 8 minims of *adrenalin* (1 to 1000).

<sup>1</sup> Journal of the American Medical Association, August 24, 1907.

<sup>2</sup> Ergebnisse der Physiologie, v, p. 698; Abst., Journal of the American Medical Association, September 28, 1907.

<sup>3</sup> Practitioner, May, 1907.

Gibbon<sup>1</sup> in an article on *postoperative treatment*, recommends a hypodermic of morphine after any operation of magnitude or long duration, or where he expects much after-pain. He found that, so far from causing vomiting after operation, the morphine lessened the tendency, and that patients were more comfortable and returned to consciousness more quiet. He prefers giving the drug before or during anesthesia in order that the patient will not learn the comfort which comes from it. Harte stated that for years he had been in the habit, before nearly all operations, of giving  $\frac{1}{4}$  of a grain of morphine and  $\frac{1}{150}$  of a grain of atropine. He has never seen any harm from this plan.

**Nitrite of Amyl.** The treatment of *hemoptysis* by means of amyl nitrite has attracted considerable attention both from the clinical and the experimental side. It was first believed that the beneficial effects produced by the drug were due primarily to a dilatation of the superficial capillaries, and secondarily to lessened cardiac action because of this dilatation. This lowering of pressure in the general circulation was given as the cause of the hemorrhage stopping. From experimental observations Pit and Petitjean assert that the inhalation of amyl nitrite causes a dilatation of the vessels of the general circulation and an actual constriction of the pulmonary vessels. Thus if the lung of an animal is exposed and amyl nitrite is administered, the pulmonary tissue is seen to become blanched simultaneously with the fall in the systemic arterial pressure.

In addition to its value in promptly stopping pulmonary hemorrhage, Grace-Calvert<sup>2</sup> credits amyl nitrite with two additional favorable factors. He states that it does not produce a reactionary pulmonary hyperemia and that it does not stop the cough. The last point is of considerable importance, as it is extremely necessary not only to get rid of the effused blood, but also prevent its being spread downward into healthy lung tissue. During the past year I have seen three cases of acute miliary tuberculosis of the lungs which apparently had their origin in this way.

Francis Hare, who originally introduced the amyl nitrite treatment of hemoptysis, reports<sup>3</sup> some 34 cases in all but 1 of which the bleeding was promptly controlled after doses of from 3 to 9 minims.

Reissmann<sup>4</sup> reports its use on 46 occasions and in 38 of these the hemorrhage ceased immediately or within one minute. He advises that a patient who is subject to pulmonary hemorrhages or one in whom such an accident is apt to occur, should carry an amyl nitrite pearl about with him. Abrams<sup>5</sup> states that, in his experience, if the first inhalation is not efficacious subsequent administration does no good. While the drug does not always control hemorrhage, Abrams believes it to be the

<sup>1</sup> Annals of Surgery, August, 1907.

<sup>2</sup> Lancet, April, 1907.

<sup>3</sup> Lancet, 1906, ii, p. 1435.

<sup>4</sup> Australasian Medical Gazette, September 20, 1906.

<sup>5</sup> Lancet, 1906.

most efficient remedy we at present possess. Brown<sup>1</sup> recommends the use of a blood-pressure instrument when using the nitrites in the treatment of pulmonary hemorrhage, in order that undue lowering of the blood pressure may be avoided.

Keith<sup>2</sup> reports a case of severe *uterine bleeding*, following labor, which was promptly arrested by the inhalation of amyl nitrite.

When used for the purposes mentioned above, the amyl nitrite is best given in pearls containing 3 to 5 minims. The pearl is crushed in a handkerchief and the fumes inhaled. Patients should be warned that it will cause a feeling of fullness in the head. If amyl nitrite is not available, a similar action can be obtained by the hypodermic use of  $\frac{1}{8}$  grain of nitroglycerin.

**Novaspirin** is a new preparation resembling aspirin. It is a combination of methylene citric acid and salicylic acid, while aspirin is composed of acetic acid and salicylic acid. Lehmann<sup>3</sup> thinks the new preparation is superior, as it is less apt to cause gastric symptoms. The dose is from  $\frac{1}{2}$  to 1 drachm. While it acts less rapidly than aspirin, the effect lasts longer.

Lehmann has used novaspirin in *influenza*, *neuralgias*, *headaches*, and *nervous dysmenorrhœa*.

**Phenol.** The treatment of *phenol poisoning* by the use of the soluble sulphates (Epsom or Glauber's salts) has long been believed to be the most efficient means we possessed. The soluble sulphates have been administered with two objects in view: one, the formation of insoluble sulphocarbolates; the other, a purgative action which washes out the bowel. Evidence based upon experimental work has been somewhat contradictory, and it was for this reason that Sollmann and Brown<sup>4</sup> attacked the subject anew. Their experimental work showed very clearly that: (1) Chemical combination between phenol and sulphate does not occur outside the body, neither in neutral nor in weakly acid nor in weakly alkaline solution. This excludes at once all possibility of chemical combination in the alimentary canal or in the blood. (2) The blood pressure and convulsive effects of phenol are not modified in the slightest degree by intravenous injection of liberal quantities of sodium sulphate under any of the following conditions: (a) When phenol, even in sublethal doses, is introduced into the stomach, and is followed within fifteen minutes by intravenous sulphate injection. (b) When sublethal doses of phenol are injected intravenously, and followed promptly by the sulphate. (c) When sublethal doses of phenol are injected intravenously after the sulphate injection. (d) When an incubated mixture of phenol, sodium sulphate, and sodium

<sup>1</sup> American Journal of the Medical Sciences, August, 1906.

<sup>2</sup> British Medical Journal, October 27, 1906.

<sup>3</sup> Deutsch. med. Wochenschrift, March 7, 1907.

<sup>4</sup> Journal of the American Medical Association, March 23, 1907.

bicarbonate is compared with a solution of phenol in sodium chloride solution. (e) When the sulphate is injected immediately after cardiac stoppage from lethal doses of phenol. The authors believe, however, that the intravenous or subcutaneous injection of a saline is of distinct value clinically, although it was not very striking in their animal experiments. Since it is harmless it should always be done in association with lavage. The sulphate may be used for this purpose in the quantity of from 0.5 to 1 liter of a solution containing 2.3 per cent. of the anhydrous or 4.6 per cent. of the crystalline salt. The technique of making the injection is the same as that employed for the ordinary saline solution. Sollmann and Brown are of the opinion that the sulphate solution possesses no particular advantage over the ordinary sodium chloride solution.

In PROGRESSIVE MEDICINE for last year<sup>1</sup> the work of Clarke and Brown on phenol poisoning was reviewed. It will be recalled that these observers found that the most efficient treatment was immediate, abundant lavage with 10 per cent. alcohol, to be followed at once by lavage with plain water. While they believe the alcohol is of some value, they attach the most importance to a thorough washing out of the stomach by lavage. Stimulation should be used as indicated.

Acker<sup>2</sup> reports two unusual cases of carbolic acid poisoning following the use of rectal enemas. In both of these cases it was apparent that the carbolic acid had not been thoroughly mixed with the water, but had settled at the bottom of the bag. The result was that the children received, in the first few ounces, a concentrated mixture of carbolic acid. Both patients recovered.

Lennander<sup>3</sup> recommends carbolic acid in the treatment of infectious processes such as *buboes*, *leg ulcers*, *soft chancres*, *osteomyelitis*, etc. The use of comparatively weak solutions of carbolic acid for this purpose is a recognized procedure. The discovery that alcohol will counteract the local effects of phenol has led to the use of stronger solutions. Lennander applies 95 per cent. pure carbolic acid for from a quarter up to two or two and one-half minutes in soft tissues and from five to ten minutes in bone cavities. The affected part is then washed out with alcohol. The use of a strong solution is less dangerous, according to Lennander, than the weak ones, as it destroys the tissue with which it comes in contact and obliterates the bloodvessels and lymphatics, thus preventing absorption. The anesthetic action of the phenol is also an important factor in bringing about a good result in this class of cases.

Randolph<sup>4</sup> reports several cases of *erysipelas* treated by the application of pure carbolic acid, and controlled by alcohol. This method of treat-

<sup>1</sup> December, 1906, pp. 279, 326.

<sup>2</sup> Archives of Pediatrics, May, 1907.

<sup>3</sup> Beiträge zur klinischen Chirurgie, 1907, vol. li, Nr. 1.

<sup>4</sup> Washington Medical Annals, March, 1907.

ment must be instituted early, before secondary infection of the deeper tissues has occurred.

In the treatment of *burns* and *scalds*, Moran<sup>1</sup> recommends the following formula:

	Per cent.
Phenol . . . . .	1
Balsami peruviani . . . . .	5
Olei ricini . . . . .	94

Pieces of gauze or cotton are soaked in this mixture and applied to the affected part. The dressing should be applied once daily. (See also Picric Acid for treatment of burns.) The local application of carbolic acid, even in weak solutions, if kept up for too long a time, is not without danger. In 1900 Harrington collected a series of 132 cases, 18 of which were observed by him, in which he showed that an aqueous solution of carbolic acid, even in the strength of 1 to 5 per cent., was capable of producing *gangrene*, when applied to a finger or a toe in the form of a moist dressing.

Wallace<sup>2</sup> has recently reported 9 cases of *gangrene* following the local use of carbolic acid. In several instances pure or very strong solutions of the acid had been used, but in 5 the strength was not more than 5 per cent. In these cases the skin was at first dry, wrinkled, and grayish white in color; later it became shrivelled and darker. The line of demarcation was marked by some hyperemia as it began to form. Amputation should not be done until the line of demarcation is distinct. Why some individuals are thus affected and others escape is not known. As this use of phenol may result in the loss of a finger or a toe it should never be used as a local dressing in any strength.

**Picric Acid.** The *Therapeutic Gazette* for June, 1907, contained a series of articles on the treatment of *burns* contributed by the following writers: Estes, Lathrop, Urmson, Cannaday, Biddle, and Swaving.

While there were individual preferences in matters of detail, the essential principles in the treatment of burns may be stated as follows: If the burn is extensive and associated with shock, the latter condition must be met first. Shock is treated in the usual way, with stimulants and saline transfusion. Two of the writers caution against the use of alcohol. Opiates must be used if the pain is severe. Clothing should never be pulled off, but cut from the affected part, and if portions of the clothing adhere they may be allowed to remain temporarily. The burned area should be cleansed as thoroughly as possible. For this purpose mild antiseptic solutions (boric acid) or normal salt solution or sterile water and green soap may be used. If blebs are present they should be punctured, but the elevated epidermis should be allowed to remain. In burns involving the fingers, toes, eyelids, and

<sup>1</sup> Virginia Medical Semi-Monthly, March 22, 1907.

<sup>2</sup> British Medical Journal, May 11, 1907.

neck and chin, care must be taken to keep the raw surfaces apart, otherwise adhesions may result.

So far the management of these cases differs but little from that of an ordinary lacerated or contused wound. In regard to the best form of dressing, opinion varies. Lathrop, Swaving, and Urmson largely depend on dressings soaked in picric acid solutions (1 per cent. or nine-tenths of 1 per cent. in water). Estes also uses picric acid in superficial burns. Strips of gauze are soaked in the picric acid solution and laid over the affected area; over this is placed a thin layer of absorbent cotton and the whole is held in place by a gauze bandage. This is left on for two days. With slight burns this is all that is necessary. In more severe burns the dressing is removed at the end of two days, by soaking it in the picric acid solution and then reapplying. The yellow stain caused by the picric acid may be removed from the hands by the use of alcohol, or rubber gloves may be worn.

When the burn is very deep or very extensive, the picric acid must be used cautiously to avoid poisoning. In these cases the dressing is changed in twenty-four hours and a powder such as aristol (Urmson) is used. When the burns are deep and there is later much necrotic tissue the wound may be treated by multiple short incisions through the diseased area (Estes), by a bichloride immersion bath of the affected part (Urmson), or by thorough cleansing daily with carbolic acid solutions. Burns with much destruction of tissue usually require skin grafting before healing finally takes place. Lathrop, however, claims that indolent and non-healing surfaces are best treated with resin cerate (*ceratum resinæ*, U. S. P.), and that under its use skin grafting is rarely necessary.

Kindleberger<sup>1</sup> recommends the picric acid method as the best one that can possibly be used in the treatment of burns. He states that in his experience it has been clearly shown that picric acid should be the method of choice, no matter how severe or extensive the burn may be. Under its use one gets a clean wound, rapid healing, diminished fever, and lessened scarring.

It frequently happens that in patients submitted to this treatment the urine is dark red and frothy when passed. This is attributed to hemoglobinuria and some carboluria, but as frequent urine analyses show no albumin the discoloration is regarded as being insignificant. In those who have both discolored urine and fever, magnesium sulphate, in small doses, may be given for its antidotal and purgative effect.

Biddle is not impressed with the value of picric acid. He states that he has now treated some 3000 cases of burns and that for twenty-three years has been using the following preparation:

<sup>1</sup> Military Surgeon, 1907.

Carbonate of lead . . . . .	1 pound
Powdered acacia . . . . .	6 ounces
Bicarbonate of sodium . . . . .	3 drams
Linseed oil sufficient to make a thick, creamy paste.	

This paste is spread on lint or cotton flannel and cut into strips. The strips are then applied to the burned surface after the blisters have been cut open, shreds of cuticle removed, and the part washed with soap and water as thoroughly as possible. The first dressing is permitted to remain until saturated with the secretions from the wound. Dressings should not be changed any oftener than necessary. Carron oil should never be used.

During the acute stages the emunctories should be kept active and the patient put on a liquid diet. Later during convalescence tonic treatment (iron, arsenic, quinine) is useful.

**Quinine.** While *malaria* has disappeared from the northern zones as an endemic disease it still remains one of the most important diseases Southern practitioners have to treat. Nor has it entirely lost its importance for those practising in the North. As Sir Patrick Manson pointed out in the Lane Lectures in 1905, our extensive and growing relations with the islands of the Pacific lends a special interest to malaria. Although with malaria as with syphilis a cure is obtained by means of one specific drug, each man has his favorite preparation and method of administering it.

For the ordinary case of malaria the result of a benign tertian infection, the administration of quinine "in adequate doses, in a proper form, at a proper time, and during a considerable period" is usually efficient.

The following plan is recommended by Vanderhoof:<sup>1</sup>

In order to promote absorption the drug should be preceded, when possible, by calomel and a saline, in order to thoroughly empty the alimentary canal. This is particularly important in bilious or remittent fever. The diet should be made up of soft articles of food, and as long as fever is present a liquid diet alone is preferable.

Owing to the extremely bitter taste of quinine its use in solution is not always possible, particularly in children. There is no doubt, however, that when given in solution the quinine is more rapidly absorbed and hence more efficient. Vanderhoof recommends that the drug be given as follows:

Sulphate of quinine, gr. v; dilute hydrochloric acid, 5 minims; water, 1 dram. When given in pill form it should be seen that the pills are freshly made, otherwise they may pass through the intestinal tract unchanged. Another method of administering quinine which Vanderhoof has found useful is to give it in soft gelatin capsules. He states that the solubility of the drug is materially aided by giving 10 minims of a dilute mineral acid a few minutes after the capsule.

<sup>1</sup> Journal of the American Medical Association, April 20, 1907.



In the management of the ordinary case of malarial fever, such as is met with in our Southern States, Vanderhoof recommends the following plan: 5 grains of the sulphate of quinine every four hours, or 20 grains a day for the first five days; then  $2\frac{1}{2}$  grains every four hours or 3 grains three times a day, for two and a half to three weeks. In severer cases larger doses (30 to 40 grains) may be given. If possible he administers 10 to 15 grains five hours before the expected chill. If the patient is seen directly after the rigor and another is not expected for two days the administration of the quinine had best be started as outlined above.

Vanderhoof particularly emphasizes the importance of rest in bed during the active stage of the disease and the use of small doses of quinine for some weeks after the disappearance of symptoms.

For internal administration, R. Howard<sup>1</sup> recommends the *hydrochloride of quinine*, as it contains a large percentage of quinine and is soluble in its own weight of water. Because of its ready solubility it is hardly likely that, even if given in tablet form, it would pass undissolved through the intestines. Despite the fact that the sulphate is the most widely used salt of quinine, Howard has shown that the sulphates have a smaller alkaloidal content than the other salts. Furthermore, the sulphates possess an additional disadvantage in that they carry considerable sulphuric acid into the stomach and so cause indigestion.

The hydrochloride, in addition to being the most preferable salt for oral administration, is also the salt most commonly used for hypodermic administration.

*Malignant or pernicious malaria* is rarely encountered in the northern zones at the present time, and when seen is usually imported from the tropics. In these malignant types of the disease the all-essential point is the introduction into the system of quinine in a manner which will ensure rapid absorption. For this purpose the quinine has been given hypodermically, by rectum and intravenously, as proposed by Baccelli. The two latter methods are not often used.

Recently several surgeons in the Indian Medical Service<sup>2</sup> have given their experience with the *hypodermic method* of treating malaria.

The objections which have been urged against the hypodermic use of quinine, namely, that it is painful, that it is prone to produce abscesses, and that *tetanus* may result, do not seem to have been borne out by the experience of these men. Of the quinine salts those most readily soluble are the hydrochloride, the hydrobromide, and the bimuriate of quinine and urea. One of these writers (L. B. Scott) expressed a preference for the hydrochloride, which dissolves in distilled water in the proportion of 1 to 1 or 1 to 2, so that a dose of 10 grains can be readily given in a 20-minim hypodermic syringe. Scott insists on absolute cleanliness both as to the needle and the patient's skin. Moncrieff used the hydro-

<sup>1</sup> Lancet, April 30, 1907.

<sup>2</sup> Indian Medical Gazette, March, 1907.

bromide in a solution of 1 grain to 7½ minims of water. The amount of water is excessive, but permits of sterilization by boiling without precipitating the salt. Probably the best site for the intramuscular injections is in the gluteal region.

Moncrieff<sup>1</sup> is of the opinion that *children* require relatively much larger doses of quinine than adults, and recommends that infants of one year should usually receive 8 to 12 grains of the sulphate or 10 to 14 grains of the bisulphate daily. He also states that quinine is more easily given to infants by hypodermic injections than by mouth, provided the needle is very sharp and the caliber is small. He recommends the fine Shimmel needles sold by Parke, Davis & Co.

Contrary to the generally accepted opinion, neither of these observers believe that quinine is as rapidly absorbed when given hypodermically as when given by mouth. Moncrieff states that the longer continuance of the fever, the comparative absence of cinchonism, the slow excretion of the quinine, and the not infrequent persistence of irritation at the site of the injection, all favor the view that quinine is slowly absorbed when given hypodermically. If this view is correct the hypodermic method should be used only when the exhibition of the quinine by mouth is contra-indicated. Scott does not think acute cases are as quickly impressed with the effects of the quinine when given hypodermically as when given by mouth. The hypodermic method, in his opinion, has its greatest field of usefulness in the administration of quinine for prophylactic purposes and as a means of preventing relapse after an acute attack.

In regard to the development of *tetanus* after the hypodermic use of quinine, McCampbell<sup>2</sup> has made an experimental study with negative results. He comes to the conclusion that the majority of cases in which tetanus has resulted after hypodermic injections of quinine can be traced to some fault in the surgical technique or to contamination of the solution of quinine. In a published inquiry he received a few replies and in only one was it reported that tetanus had succeeded the injection. In this case the evidence was not at all conclusive, as there were several slight abrasions which might have served as points of entrance.

Manson<sup>3</sup> states that if tetanus follows the injection of quinine it is due either to a contaminated needle or a foul solution.

An ever-recurring subject is the question of the influence of quinine on the production of *malarial hemoglobinuria*. Some believe that the hemoglobinuria is produced by quinine, while others are equally insistent that the quinine is in no way responsible.

This attitude is illustrated by two articles, published during the past

<sup>1</sup> Loc. cit.

<sup>2</sup> Journal of the American Medical Association, March 16, 1907.

<sup>3</sup> See Lane Lectures, 1905.

year, by Ketchen<sup>1</sup> and Brem<sup>2</sup> in which entirely divergent opinions are expressed.

Ketchen cites a case in which it seemed to be proved undoubtedly that the administration of quinine, even in small doses, was invariably followed by hemoglobinuria. In this instance the patient had been free from any acute attack of blackwater fever for fourteen months. Ketchen quotes the opinion of Koch and others to the effect that there is a direct relationship between the administration of quinine and the development of hemoglobinuria.

Brem reports in detail his experience with fourteen cases of blackwater fever at the Ancon Hospital in the Canal Zone. His conclusions are as follows:

1. A febrile affection resembling the estivo-autumnal type of malarial fever was the only etiological factor discoverable. Previous attacks of malarial fever appeared to furnish a favorable ground. Quinine was not an etiological factor, either predisposing or exciting. Evidence appears to favor the view that the estivo-autumnal parasite, and not a special organism, is the exciting cause.

2. The symptoms and signs of the disease may be very mild and the gravity of the illness indicated only by the urine examination. A history of dark, black, or bloody urine can be obtained almost invariably.

3. The degree of fever bears no relation to the intensity of hemoglobinuria and albuminuria. A posthemoglobinuric fever of peculiar character occurred in four cases; it does not yield to quinine.

4. Blood examinations show that the primary event is destruction of the red blood corpuscles, with hemoglobinemia and subsequent hemoglobinuria. Anemia is very rapid, and the rapidity of recovery is phenomenal.

5. In well-defined cases practically an absolute diagnosis can be made from a macroscopic examination of the urine combined with the test for albumin. In borderline cases a test for hemoglobin is necessary for absolute diagnosis, but a probable diagnosis can be made from a deeply colored urine with a brownish sediment and albumin 20 per cent. or more.

6. The mortality was 14.3 per cent. in the series.

7. A correct prognosis in individual cases is difficult.

8. Intramuscular injections of quinine appear to act specifically. The best method is thought to be the injection of 10 grains every four hours during the first forty-eight hours (15 grains may be substituted for the first three or four doses) and then smaller doses by mouth may be given if vomiting does not forbid. Quinine bihydrochloride in an excess of acid is more suitable than quinine bimuriate with urea for intramuscular injection.

<sup>1</sup> South African Medical Record; Lancet, September 22, 1906.

<sup>2</sup> Journal of the American Medical Association, December 8 and 15, 1906.

In all of Brem's cases the malarial plasmodium was searched for and was found in only two cases.

According to Stephens,<sup>1</sup> parasites were found in the blood in 95.6 per cent. of cases (23), before the attack of hemoglobinuria in 61.9 per cent. of cases (63), on the day of the hemoglobinuria and on the day after, when cases are usually first seen, in only 17.1 per cent. of cases (64).

These percentages are based on the records of observers who have made notes on the relationship between blackwater fever and the malarial parasite. After a very careful analysis of the facts presented by both sides and from his own experience, Stephens states that the two main factors in the production of blackwater fever are malaria and quinine. Why quinine will at one time produce hemolysis and at another time will not remains unknown.

According to Broadbent<sup>2</sup> quinine is an excellent remedy for *influenza*, both as a curative agent and as a prophylactic. In a fully developed attack of the disease Broadbent prescribes 1 dram of ammoniated tincture of quinine (B. P.) and 2 drams of liquor ammoniæ acetatis every hour for three hours and then every four hours.

As a prophylactic he states that 2 grains of quinine every morning during the prevalence of an epidemic are efficient. He cites an instance in which in a large school for girls a prophylactic dose of quinine was ordered for each of the pupils and the teachers, but the servants were forgotten. Nearly all of the pupils and teachers escaped, while all of the servants succumbed to the influenza.

For the relief of *coryza*, Waxham recommends the following:

R—Quininæ salicylatis . . . . .	gr. iss
Acidi arsenosi . . . . .	gr. 1½
Ext. belladonnæ . . . . .	gr. ⅓
Capsici . . . . .	gr. ¼

Two capsules of this composition every hour for three hours, and then one every four hours.

Quinine at one time was quite extensively used to stimulate feeble *uterine contractions*, but of late years has been pretty generally abandoned by obstetricians. Mäurer,<sup>3</sup> from a clinical study of its effects as an oxytocic, concludes that quinine undoubtedly strengthens the uterine contractions, and perhaps may induce their onset, but that it shares, with other drugs of this class, the disadvantage that its effect cannot be guaranteed in every case.

His method of administration is to give 15 grains of the sulphate of quinine by mouth; at the end of an hour, if no effect is manifest, 7½ grains are given. If the latter dose fails to produce any effect it is

<sup>1</sup> Osler's Modern Medicine, vol. i, p. 449.

<sup>2</sup> Practitioner, January, 1907.

<sup>3</sup> Deutsch. med. Wochenschrift, January, 1907.

repeated in half an hour, but if this is ineffectual it is abandoned as useless.

In 63 cases of labor and 15 cases of abortion Mäurer claims to have obtained satisfactory effects in 78.2 per cent. of the cases.

**Salicylate of Sodium.** Several very interesting articles have appeared on the use of the salicylates in acute articular rheumatism. Phillips<sup>1</sup> and Clarke<sup>2</sup> advocate massive doses, averaging 200 grains daily. The former urges the free use of water to favor elimination and a preliminary dose of calomel, followed by a saline and later the use of cascara to ensure the bowels being freely opened. If sweating is annoying the patient should be sponged with water to which sodium bicarbonate has been added. In the beginning a milk diet is the best, although, if not well borne, soups, broths, or well-cooked rice or tapioca may be substituted. When the fever subsides the diet should be liberal in order to counteract the great tendency to anemia.

† In administering the salicylate of sodium Phillips recommends the following plan: 20 grains of sodium salicylate every hour until the patient becomes toxic, the total amount not to exceed 200 grains. If this amount of the drug has not produced toxic symptoms and the disease has not yielded to treatment, he continues giving the salicylate in 20-grain doses, watching carefully for evidences of toxic symptoms. In some cases as much as 300 (Phillips) or 360 grains (Clarke) may be taken. The toxic symptoms noted are ringing in the ears and deafness.

The salicylate should be well diluted and 10 to 15 grains of sodium bicarbonate given with each dose. Both authors state that these massive doses rarely produce any gastric disturbance (nausea, vomiting).

Local treatment of the joints is unimportant, except in so far as it adds to the comfort of the patient. In the acute stages the joints may be painted with wintergreen oil and wrapped in thick cotton wadding or the local pain may be combated with hot stupes of lead and opium or by the application of menthol and oil of wintergreen ointment.

When the acute symptoms have subsided the salicylate should be continued in 15- to 20-grain doses three times a day. Furthermore, the patient should be kept in bed in the recumbent posture for three weeks to avoid cardiac complications.

Phillips states that, in children, subsequent attacks may be avoided by the administration of small doses of salicylate of sodium one week out of each month and continuing this for at least one year.

Clarke's method differs but little from that recommended by Phillips. He gives 10 to 20 grains every hour while the patient is awake. At the first evidence of toxic symptoms the drug is stopped and again given in the same doses, but at two- to four-hour intervals. With each recurrence of the toxic symptoms the drug is temporarily stopped.

<sup>1</sup> Cleveland Medical Journal, December, 1906.

<sup>2</sup> American Journal of the Medical Sciences, September, 1906.

Whether the salicylates act as bactericides or antitoxins is, as Stockman<sup>1</sup> points out, an unsettled question. He advocates the early use of large doses of salicylate of sodium because the drug has a more rapid and a more certain effect on the disease while the specific cause is in the blood stream and fluid of the joints. When the heart valves or fibrous tissue becomes involved the salicylates are not nearly so effective, due, Stockman believes, to the fact that the drug has difficulty in penetrating these tissues. He states that the rapid action of the salicylates on the pain and swelling of the joints is explainable on the ground that large amounts of the drug are excreted into the joint cavity from the blood. This, he says, can readily be shown by its detection in the fluid withdrawn by means of a hypodermic syringe.

In last years review<sup>2</sup> attention was directed to an article by Langmead in which he reported a series of eight cases of poisoning in children, from the use of large doses of salicylates. In these cases the toxic effects resembled diabetic coma. An editorial article<sup>3</sup> has called attention to the interesting point that these symptoms can, as a rule, be promptly controlled by stopping the salicylate and administering full doses of bicarbonate of sodium. From the articles just reviewed it seems to be clearly demonstrated that unusually large doses of the salicylates can be administered with safety providing the eliminative organs are stimulated and at the same time full doses of sodium bicarbonate are given.

Innumerable untoward effects have been credited to the salicylates, but rarely of a fatal character. Leach<sup>4</sup> has recently called attention to instances of nose-bleed occurring during the course of influenza. He is of the opinion that the bleeding was an evidence of salicylism. According to H. A. Hare, the salicylates share with quinine and the iodides the distinction of producing untoward and undesirable effects more often than another drug.

It should be borne in mind that individuals suffering from middle-ear disease should not be given the salicylates unless urgently demanded, as their deafness is often made permanently worse. The drug is not markedly a cardiac depressant, but it should be used with care when administered to persons with a weak heart.

**Sparteine.** In last year's review attention was directed to an article by Petty<sup>5</sup> in which he stated that the usual dose of sparteine, as recommended by most of the text-books, is far too small to be of any benefit. McGuire<sup>6</sup> emphasizes this point. He states that within the past five

<sup>1</sup> British Medical Journal, November 24, 1906.

<sup>2</sup> PROGRESSIVE MEDICINE, December, 1906.

<sup>3</sup> Therapeutic Gazette, 1907.

<sup>4</sup> British Medical Journal, April 20, 1907.

<sup>5</sup> PROGRESSIVE MEDICINE, December, 1906.

<sup>6</sup> American Journal of Surgery, February, 1907.

years he has lost more cases from *post-operative suppression of urine* than from all other causes combined. Having met with failure in the use of the commonly recommended diuretics he tried sparteine with excellent results. He reports six cases in which the diuretic action was marked and in addition the rapidly acting heart was favorably influenced.

Maguire recommends the administration of from 1 to 2 grains hypodermically and that the dose be repeated every three to six hours.

**Strophanthus.** It was pointed out in the section on digitalis that the only objection to that drug was the unreliability of its preparations. Hatcher<sup>1</sup> has made a study of samples of the tincture of strophanthus. The various specimens were not obtained from the better class of stores, but in most cases from those in the poorer quarters of New York City. He found that there is not the slightest difficulty in obtaining a tincture of strophanthus in the open market of quite as nearly uniform potency as obtains in the case of tinctures of other drugs which are not standardized. It is in this uniformity of its action that strophanthus possesses a distinct advantage over digitalis. Digitalis preparations if reliable are superior to strophanthus in cardiac conditions. It should be remembered, however, that strophanthus often acts exceedingly well in certain instances where digitalis fails; this is particularly true of children.

Starck<sup>2</sup> reports excellent results in the treatment of failing compensation from intravenous injections of *strophanthin*. The average dose he employed was 1 mg. ( $\frac{1}{8}$  grain).

Strophanthus is usually credited with relieving cardiac dropsy through its action on the heart and not because of any diuretic properties it possesses. Starck mentions two cases, however, in which the intravenous injection of strophanthin increased the urinary output from 300 and 700 c.c. to 3000 c.c. in twelve hours.

**Sulphate of Magnesium.** Knowledge of the extraordinary action of sulphate of magnesium in the production of *anesthesia* is due to the experimental work of Meltzer. Basing his theory on the fact the sodium and calcium salts have been shown to have distinct stimulating properties for some of the functions of the animal organism Meltzer reasoned that the magnesium salts, which are found plentifully in the tissues, might possibly have an inhibitory action on these same functions.

Working on this hypothesis he undertook a series of experiments in association with Auer. They found that the subcutaneous injection of solutions of magnesium sulphate was capable of producing a deep and often long-lasting anesthesia; that intravenous injections effected the centres of the medulla oblongata with depression of the respiratory and deglutition centres, but with no apparent effect on the cardiac mechanism; that direct application of the solution to the nerve trunks blocked both afferent and efferent stimuli, the functions of the nerves being quickly

<sup>1</sup> Journal of the American Medical Association, April 6, 1907.

<sup>2</sup> Deutsch. med. Wochenschrift, xxxii, Nr. 11.

restored, however, when the magnesium salt was washed away. Finally it was shown that in monkeys intraspinal injections of a magnesium sulphate solution was capable of producing general anesthesia. This last observation led Meltzer to recommend intraspinal injections of magnesium salts in man for purposes of general anesthesia. For producing general anesthesia 1 c.c. of a 25 per cent. solution for each 20 pounds body weight was used. Thus far fourteen cases are on record in which this method has been employed (Blake). Based on observations made in these cases, the following phenomena were observed: There was muscular relaxation and anesthesia with loss of the tendon reflexes. The respiration was usually slowed and the temperature generally was elevated from 100.6° to 105° F.; the rise in the temperature occurred on an average twenty-two hours after the injection. Retention of urine was noted in twelve of the fourteen cases. Disturbance of the cardiac rhythm was noted but once. The most serious of the untoward effects was undue slowing of the respiration sometimes requiring artificial respiration. Washing out the spinal canal with normal salt solution was very effective in relieving the respiratory difficulty.

The extreme nervous excitability and intense muscle spasm incident to *tetanus* led Meltzer to recommend intraspinal injections for this condition.

Robinson<sup>1</sup> has reported a case of tetanus successfully treated by this method and has collected five other cases from the literature. In Robinson's case the following procedure was followed: Lumbar puncture was performed and the spinal fluid allowed to escape. 1 c.c. of a 25 per cent. solution of sulphate of magnesium for about each 20 pounds of body weight was then quickly injected. Three such injections were made and were followed in each instance by the greatest relief. Within a few minutes the rigidity of the affected muscles lessened and soon became entirely relaxed. There was a return of the symptoms after the first injection, in about twelve hours. The second injection was given about eighteen hours after the first. The good effects of the second injection lasted about three days when, with a return of the symptoms, the third and last one was given. Absolute quiet and sedatives (bromide and chloral) are used in conjunction with the intraspinal injections.

Of these six cases reported by Robinson (five from the literature and one his own) recovery occurred in three. It is extremely interesting to note that one of the cases that recovered was one of acute tetanus in which antitoxin had been used without success. Recovery from acute tetanus (that is development of the disease within nine days after an injury) is extremely rare. Tetanus antitoxin has been unavailing in these cases, for once the union between the toxin and higher nerve centres takes place death almost always follows. Chronic tetanus, on the other

<sup>1</sup> Journal of the American Medical Association, August 10, 1907.



hand, not infrequently ends in recovery. The failure of every other method in dealing with acute tetanus should lead to as thorough a trial as possible with the magnesium salts. In reporting cases of tetanus it is desirable that, whenever possible, the incubation period be given.

Another application of the magnesium salts, quite as extraordinary as the results just given, is their external use in *acute inflammatory conditions* associated with pain. Tucker<sup>1</sup> was led to this use of the salts from the observations of Meltzer. The technique he employed was as follows: The application consists of a saturated solution of magnesium sulphate in water. The solution is applied on from 15 to 20 thicknesses of ordinary gauze. This is saturated with the solution at least every half-hour, or as often as necessary to prevent drying, depending on the time of the year and the temperature of the room. The gauze is not removed until the end of twenty-four hours; the parts are then washed with water and the dressing reapplied if necessary. There is then found to be a marked blanching of the surface which is, however, not followed by any deleterious effects. The remarkable anesthetic properties of the solution was shown from the fact that the attendants who made the applications experienced a partial loss of sensation accompanied by tingling of the arms and hands. This persisted for from twelve to twenty-four hours. The conditions in which Tucker used the applications of magnesium sulphate were *gonorrheal epididymitis*, other painful affections of the testicle, various painful joint conditions (*acute rheumatism, gonorrheal arthritis*), *erysipelas, neuritis, sprained ankles*, and *simple contusions*. The applications always relieved the pain in a few hours. Swelling of the testicle and redness and swelling of a joint usually subsided in from twenty-four to thirty-six hours.

**Thyroid Extract.** Howard<sup>2</sup> has made an elaborate analysis of seventy-six cases of *myxedema*. In regard to treatment he quotes Byrom Bramwell to the effect that it is no exaggeration to say that the cure of myxedema by thyroid treatment is one of the greatest therapeutic achievements of this or of any age.

The most convenient way to administer the thyroid is in the form of tablets. Howard states that the first thing to determine is the most suitable constant daily dose; this can be done only by trial and must be determined for each case. It is best to begin with a small dose (one 5-grain tablet, or 2 grains of the extract) once a day, and gradually increase in frequency and in amount until the symptoms begin to subside. In cases in which the disease has lasted for some years, in the aged and in those who show any indication of arterial or cardiac degeneration the greatest care must be exercised during this stage. Rest in bed for a time, should be insisted upon so that the heart and arteries are sub-

<sup>1</sup> Therapeutic Gazette, April, 1907.

<sup>2</sup> Journal of the American Medical Association, April 27, 1907, p. 1407.

jected to as little strain as possible. Sudden overexertion should be avoided, as cases of sudden death have been reported.

The first stage of treatment should be kept up for from six to twelve weeks for the advanced cases.

Overdosage is indicated by undue acceleration of the pulse (an increase of 10 to 20 beats per minute), a rise of temperature of  $1^{\circ}$  above normal; vomiting or purging, extreme prostration, headaches, sweating, and irritability sometimes occur and form a combination similar to the toxic symptoms of exophthalmic goitre. In some cases there is intolerance for even 1 grain a day.

After the first course of treatment, which lasts from six to twelve weeks, the frequency may be reduced and the minimal dose ascertained. The symptoms may be kept in abeyance in some cases with one tablet a day; in others one tablet every two or three days is sufficient. If the thyroid is entirely discontinued there may be a return of the symptoms; this occurred in three of Howard's cases.

The effect of thyroid extract on myxedema is extraordinary. Howard states that the first effect is a return of the temperature to the normal. Next there is a gradual or even a sudden diminution in the subcutaneous edema, with a consequent loss in body weight. The skin loses its dry, harsh appearance and becomes soft and moist. The hair begins to grow in the form of a fine thick crop over the scalp, pubes, and axillæ. The urine sometimes increases in quantity and the albuminuria and cylindruria disappear. The menses also return to their normal regularity and quantity. The anemia is for a time unaffected and may even grow worse, but this soon improves as the patient gains strength and improves.

In addition to the marked change in the physical appearance of the patient there is also a corresponding improvement in the mental and nervous symptoms. The mind becomes active, the expression brightens, and the patient evinces an interest in his or her surroundings and affairs of life. Actual insanity has, in some cases, been cured.

Rugh<sup>1</sup> reports a case of *hemophilic knee-joint* treated by incision under the supposition that it was of an inflammatory nature. Bleeding after the operation was very profuse and the commonly employed styptics did not control the constant oozing. The patient meanwhile became very anemic. The administration of thyroid extract in 5-grain doses three times a day at once caused a diminution in the amount of blood lost and also relieved the pain, which had been severe. In eight days the bleeding had ceased. Five months later the man was perfectly well and had had no recurrence.

**Trypsin.** The treatment of malignant growths by means of trypsin has excited considerable interest during the past eighteen months. Opinions as to its value vary greatly, although all observers urge that it

<sup>1</sup> *Annals of Surgery*, May, 1907.

be given a thorough and impartial trial. This method of treating cancerous growths owes its origin to Dr. John Beard, of the University of Edinburgh. According to Beard, cancer cells differ from other cells only in the characteristic that they are latent and have not been modified in the course of embryonal development. In those who later develop cancer these latent or unmodified cells, located in various parts of the body, are stimulated and under favoring circumstances produce a malignant growth. In this respect Beard's theory closely resembles Cohnheim's inclusion theory. The efficiency of the theory rests on the fact that these latent or asexual cells owe their existence to the absence of some internal substance whose function is to destroy these aberrant cells or to convert them into normal types.

From the fact that these aberrant cells disappear in fishes when the pancreatic function is established Beard believes that it is in the use of pancreatic juice or its active principles that cancer may be successfully attacked in man. At present there is considerable uncertainty in the matter of dosage. Beard has recently recommended 20 minims daily. Morton<sup>1</sup> has reported twenty-nine cases, most of them in an inoperable condition, in which trypsin injections have been employed with a fair degree of success. He also gives details as to dosage, etc. The various preparations of pancreatic juice are: *injectio trypsinii*, *injectio amylopsini*, *lotio pancreatis*, trypsin powder, and holadin. In this country the pancreatic preparations of Fairchild Bros. & Foster have been usually employed. Morton started with 5 minims of the *injectio trypsinii* and increased it 5 minims daily up to 20 minims. He states that in the present uncertain state of our knowledge the dose must be governed largely by the general reaction and the local effect on the tumor. Campbell,<sup>2</sup> who reports a successful case, started with 5 minims of the *injectio trypsinii* and increased 5 minims every third day. Later 60 minims (one ampulla) diluted with two volumes of sterile water were injected every other day. Graves<sup>3</sup> began with 10 minims and later increased the dose to 40 minims three times a week.

The method of administering the trypsin varies. The most usual method and the one recommended by Beard is the injection of the trypsin in the subcutaneous tissues, preferably the buttocks. All but one of Morton's cases were treated in this way. Graves expresses the opinion that the injections must be made directly into the cancerous node. He found that the node thus injected shrank, became hard and finally disappeared, but that neighboring nodes were but little affected. Von Leyden and Bergell<sup>4</sup> claim that larger amounts of trypsin pass into the blood when administered by mouth than when given subcutaneously.

<sup>1</sup> Medical Record, December 8, 1906.

<sup>2</sup> Journal of the American Medical Association, January 19, 1907.

<sup>3</sup> Boston Medical and Surgical Journal, January 31, 1907.

<sup>4</sup> Zeitschrift f. klin. Medizin, 1907, lxi.

They are not impressed with the results obtained by injecting the trypsin directly into the cancerous area. Given by mouth no marked results were obtained in the case of inaccessible tumors, but when the cancerous growth involved the stomach and there were no metastases the results were remarkably good.

So far trypsin has not produced any serious untoward results. Reactions, however, are not unusual. Morton states that these reactions may follow a dose of 5 minims. They are characterized by increased temperature, nausea, vomiting, pain in the back, drowsiness, edema, albuminuria, and high arterial tension. The tumor when visible may within six hours become red or purple, turgid, hot to the touch, and the patient may complain of pain or of a gnawing sensation. Both the constitutional, and local effects pass off in a few hours and apparently produce no ill effects.

One of the factors entering into the successful use of trypsin seems to be in the administration of amylopsin. Beard assumes that after a certain time the cancer cells of the tumor die and their removal must be promoted by the use of the injectio amylopsini. The amylopsin is devoid of the proteolytic (trypsin) and fat-splitting (lipase) ferments.

Morton states that at the present time it is difficult to determine the proper time at which to begin the amylopsin injections and also the dosage. He suggests that in beginning treatment one should feel his way with daily doses of from 20 to 30 minims of the injectio trypsin for from four to six weeks and then resort to the injectio amylopsini in 5 minim doses cautiously advanced.

~~It~~ Turpentine has long been recognized as an excellent agent to relieve *tympanites*, particularly the tympanites occurring during the course of typhoid fever. Under these circumstances the turpentine may be used in the form of stupes, in enemata or by mouth. It is also valuable during the convalescence of typhoid fever when diarrhea is present and relapses are constant and due to an unhealed state of Peyer's patches.

The following formulæ<sup>1</sup> may be used:

R̄—Olei cinnamomi . . . . .	gtt. xx
Olei terebinthinæ . . . . .	℥iv
Mucil. acaciæ . . . . .	q. s. ad ℥iv—M.

Sig.—One teaspoonful every four hours.

R̄—Olei terebinthinæ . . . . .	℥j
Olei amygdalæ (exp.) . . . . .	℥ss
Tinct. opii . . . . .	℥ij
Mucil. acaciæ . . . . .	℥v
Aquæ laurocerasi . . . . .	℥ss—M.

Sig.—One teaspoonful every four hours to relieve the tympanites.

<sup>1</sup> Journal of the American Medical Association, September 1, 1906.

The following may be used as an enema for the relief of tympanites:

R.—Olei terebinthinæ . . . . .	℥j
Olei olivæ . . . . .	℥iss
Pulv. camphoræ . . . . .	gr. xx
Mucil. acaciæ . . . . .	℥ss
Aquæ . . . . .	℥x.—M.
Sig.—Stir well and use as an enema.	

**Venesection.** Jacobs<sup>1</sup> recommends the following method for performing *phlebotomy*. He uses a needle two inches long, with a caliber of one-sixteenth of an inch. To this is attached a piece of rubber tubing four to six inches long. If desired a glass cannula may be attached to the free end of the tubing. After a tourniquet has been applied to the arm the needle is introduced through the tissues into the lumen of a vein at the bend of the elbow. The needle is introduced in a reverse direction to that of the blood current.

The advantages claimed for this method are that no incision is necessary; the procedure is clean, easy, and effectual; the amount of blood withdrawn can be measured exactly and the blood is sterile and can be used for cultural purposes.

For the past two or three years I have used this method a great deal for obtaining blood for experimental purposes. After one has gained a little experience with it very little difficulty is met with in introducing the needle. As compared to the ordinary method of bleeding, however, I do not think Jacob's method is to be preferred for clinical purposes. While not of frequent occurrence I have on several occasions experienced great difficulty in getting the needle into the vein and in several others have failed to obtain sufficient blood even when the flow was aided by an aspiration bottle. The old method of making a small incision and opening a vein is rapid and in my experience absolutely free from danger if ordinary cleanliness is observed.

Plunging the needle directly into a vein is a rapid and safe method of performing intravenous transfusion. It has been claimed that plunging the needle directly through the skin is apt to cause infection of the patient or contamination of the withdrawn blood. If such is the case I have never seen it happen.

Devoe<sup>2</sup> advocates *local bloodletting* in the treatment of *dropsy* of cardiac origin. By this method general anasarca and ascites have been greatly relieved. Devoe makes the incisions chiefly in the legs and ankles. The incisions are from one-half to three-quarters of an inch in length and are made freely through the skin down to the deeper fascia. Following the flow of blood which always occurs, a colorless serum is emitted for several days. The wounds have always healed without the formation

<sup>1</sup> American Journal of Surgery, April, 1907.

<sup>2</sup> American Medicine, January, 1907.

of a slough or other untoward occurrence. The practice of venesection has fallen so generally into disuse and the prejudice against it is so great that, as Devoe states, very few of the profession are aware of its value. In no condition is the beneficial effect of venesection more strikingly shown than in the *failing compensation of cardiac disease*. There is no measure which will so quickly relieve the dyspnea, cyanosis, and rapid, feeble heart action as bloodletting. In some instances before the bleeding has been finished the color becomes better and the intense orthopnea much improved. As a general rule it may be stated that the more threatening the condition the more striking the effects of the venesection. The bleeding should be allowed to continue until 25 or 30 ounces are withdrawn. The flow of blood usually ceases before this amount is reached, however.

**Veronal.** The occurrence of a dermatitis following the use of veronal has been reported by House<sup>1</sup> and Bulkley.<sup>2</sup> Both patients were elderly men. In one the untoward effects followed a dose of 15 grains, in the other after three 7½-grain doses at intervals of several hours. In both cases the eruption was general, though most marked on the lower extremities. "In some places, especially on the body, it was an erythematous rash, somewhat resembling scarlatina, but on the limbs it was largely in separate, flat maculo-papules, some of them nearly an inch in diameter, but most of them less than half an inch, slightly raised above the skin, like a papular erythema. The centre of most of the lesions was darker red, and some appeared hemorrhagic (Bulkley)." In addition to the cutaneous disturbance each case suffered from vertigo, depression, and mental haziness. House<sup>3</sup> does not believe veronal a safe drug for aged persons, except in small doses. He has observed several senile patients in whom the drug caused staggering, vertigo, and stupor for half a day after the hypnotic effects had worn off. In these cases trional is the preferable drug.

The usual dose of veronal is from 5 to 10 grains in a capsule or in solution.

**Yohimbin.** This drug was brought before the profession some ten years ago by Spiegel. It has been especially recommended in the treatment of *impotence*, but the results obtained have not been at all uniform. Applied locally (in a 1 to 2 per cent. solution) yohimbin produces an anesthetic effect similar to cocaine, but is less toxic. Given by mouth or hypodermically it produces a general vasodilatation of the skin, mucous membranes, and particularly of the sexual organs. In addition to this general effect Dammann<sup>4</sup> believes it has a direct stimulating action on the erectile centre. Ordinary doses of yohimbin produce

<sup>1</sup> Journal of the American Medical Association, April 20, 1907.

<sup>2</sup> Ibid., June 1, 1907.

<sup>3</sup> Ibid., June 22, 1907.

<sup>4</sup> Medizinische Klinik, 1906, Nr. 52.

an effect similar to that obtained with cocaine; larger doses also agree in their action with similar doses of cocaine.

In addition to its use in impotence in the male, Loewy<sup>1</sup> claims that yohimbin may be used to advantage in cases of irregular and scanty menstruation and in the premature occurrence of the menopause.

The drug is administered in tablets of  $\frac{1}{12}$  grain three times daily; this may be increased to two tablets three times daily.

<sup>1</sup> Therapie der Gegenwart, December, 1906





# INDEX.



**ABDOMEN**, adhesions in, due to gall-bladder infection, 102  
**Abdominal viscera**, effect of cocaine on, 32  
     of external stimuli on, 34  
**Absorption in intestines**, 21  
**Acetonuria**, 289  
**Achylia with diarrhea**, 80  
**Actinomycosis**, 304  
**Adamantine epithelioma**, 218  
**Adrenalin**, 127, 136, 252, 260, 290, 306  
     for hematuria, 230  
     to aid catheterization, 241  
**Aërophagia**, effect of, on gastric ulcer, 58  
     tension in, 18  
**Albumin in feces**, 90  
**Alcohol**, 261, 283  
     effect on stomach, 29  
**Alcoholic icterus with splenomegaly**, 110  
**Alcoholism**, 270  
**Alimentary hypersecretion**, 65  
**Anemia**, 305  
     pernicious, 296  
**Anesthesia**, 144, 244, 302, 319  
     chloroform, 147  
     ether, 148  
     ethyl chloride, 148  
     local, 146  
     nitrous oxide, 244  
     scopolamine-morphine, 144, 302  
     in obstetrics, 302  
     spinal, 145  
     sulphate of magnesium, 319  
**Angina pectoris**, 303  
**Angioma, congenital**, 207  
**Antidiphtheritic serum**, 262  
**Antidysenteric serum**, 266  
**Antigonococcic serum**, 255  
**Antimeningitic serum**, 249  
**Antiseptic drugs**, effect of, on intestines, 85  
**Antiseptics for foodstuffs**, 22  
     intestinal, 78, 84  
**Antistreptococcic serum**, 267  
**Antitetanic serum**, 267  
**Aortic incompetence, digitalis in**, 291  
**Apomorphine**, 270  
**Appendicitis and renal colic**, 230  
     and spermatic colic, 230  
**Appendicular affections**, 230  
**Arterial degeneration, experimental**, 126  
     tension in renal disease, 124  
**Arteries, renal, sclerosis of**, 121-124

**Arteriosclerosis**, 121, 304  
     diet in, 304  
**Artery, obstruction of, due to kinking in fractures**, 160  
**Arthritis, clinical picture of**, 185  
     diagnosis of, 185  
     etiology of, 182-184  
     gonorrheal, 184, 255, 321  
     in scarlet fever, 184  
     in influenza, 184  
     pathology of, 179-182  
     rheumatoid, 293  
     syphilitic, 184  
     treatment of, 186  
**Asthma, bronchial**, 306  
**Auto-intoxication of intestinal origin**, 67  
**Azoöpermia**, 251

## B

**BACTERIA**, fecal, estimation of, 79  
     in achylia, 80  
     in constipation, 81  
     in hyperacidity, 80  
     in jaundice, 81  
     in poor starch digestion, 81  
     method of detecting, 82  
     intestinal, after childhood, 69  
     at birth, 69  
     function of, 68  
     in early life, 69  
     not harmful, 69  
**Barium chloride**, 127  
**Belladonna**, 271  
**Beta-naphthol**, 87  
**Bicarbonate of sodium**, 272, 289, 318  
**Bier's hyperemia**, 140, 150, 186  
**Biliary tract, infections of**, 92  
     adhesions in abdomen in, 102  
     and gallstones, 97-102  
     bacteria in, 93  
     by common bile duct, 93  
     by direct infection, 93  
     by lymphatic circulation, 94  
     by portal circulation, 93  
     by systemic circulation, 94  
     due to typhoid, 95  
     latent or masked, 94  
     pathways of, 93  
     results of, 94  
     surgical treatment of, 106  
     treatment of, 106  
**Bismuth salicylate**, 87

- Bladder, 233**  
 cancer of, 235  
 extirpation of, 237  
 implantation of ureters in, 232  
 rupture of, 238  
 stone in, 239  
   tuberculin for, 237  
   tuberculosis of, 239  
 tumors, malignancy of, 235  
 ulcer of, 233  
   acute perforating, 233  
   diagnosis of, 234  
   prognosis of, 234  
   treatment of, 234
- Blood examination in gastric cancer, 46**  
 occult, new tests for, 51  
 oozing, from mucous membrane of stomach, 55  
 pressure in renal disease, 124  
 transfusion of, 135
- Bloodletting, 325**
- Bloodvessels, surgery of, 135, 139**  
 injury of, in fractures, 139
- Bone cysts, 217**  
 sarcoma of, 215  
   Colley's fluid for, 216, 229  
 tuberculosis of, 187, 192  
   healing of, 193  
   infiltrating, 193  
   x-rays for diagnosis in, 194  
 tumors, 215-225
- Bradycardia, 278**
- Bromoform, 273**
- Bronchial asthma, 306**
- Buboes, 309**
- Burns, 310**

## C

- CACTIN, 273, 302**  
 Cactina, 273  
 Cactus grandiflorus, 273  
 Cadaverin, 71  
 Calculus, vesical, 239  
 Callus formation, 150  
 Cancer. *See* Carcinoma.  
 Carbolic acid. *See* Phenol.  
**Carcinoma of bladder, 235**  
   of prostate, 244  
   of skin, 197  
   of stomach, 37, 43, 275  
     and ulcer, 49  
     blood in, 46  
     diagnosis of, 43-50  
     fever in, 49  
     loss of weight in, 47  
     predisposing causes, 44  
     secondary, 51  
     Solomon's test for, 47  
     symptoms of, 44, 45, 48  
     treatment of, 50, 275  
     x-rays in, 50  
   relation of, to diet, 286
- Cardiopsis, 64**
- Catheterization, adrenalin an aid in, 241**
- Cellulitis of spermatic cord, 251**
- Cerebrospinal meningitis, 266, 269**

- Cervix uteri, spasm of, 306**
- Chancres, soft, 309**
- Chemical products of intestinal fermentation, 70**  
 putrefaction of, 70
- Childhood, diarrhea of, 281**
- Children, gonorrheal arthritis in, 184**  
 quinine for, 314  
 renal tumors in, 118
- Chloral hydrate, 273**  
 poisoning, 275
- Chlorate of potassium, hematuria from, 229**
- Chloretone, 275**
- Chloride of sodium, 276**
- Chloroform anesthesia, 147**
- Cirrhosis, portal, and portal pressure, 110**
- Climate. *See* Fresh air.**
- Cocaine, effect of, on abdominal viscera, 32**
- Colic, hepatic, 306**  
 renal, 306  
   and appendicitis, 230  
   due to an anomalous artery, 230  
   spermatic, 230  
   and appendicitis, 230
- Colley's fluid, 216, 279**
- Colon, idiopathic dilatation of, 92**
- Complications of pregnancy, 297**
- Compound fractures, 155-158**
- Congenital nevi and angioma, 207**  
 pigmented moles, 205
- Connective-tissue tumors, 202-215**  
 and trauma, 204
- Constipation, 81**
- Contusions, 321**
- Coryza, 316**
- Cotarnine, 281**
- Courvoisier's law, 182**
- Coxa vara, 161, 167**  
 tuberculosa, 168
- Creosote, 281**
- Cresol, 72**
- Cystitis, 257**  
 vesiculotomy for, 257
- Cystoscopy, oxygen for, 239**
- Cysts, bone, 217**  
 of urachus, 232

## D

- Desmoid reaction, Sahli's, 26**
- Diabetes mellitus, 288**
- Diabetic coma, 289**
- Diarrhea, achylia with, 80**  
 of childhood, 281  
 of infancy, 281
- Diet, 79, 282, 304**  
 and cancer, 286  
 in arteriosclerosis, 304  
 in diabetes mellitus, 288  
 in gastric ulcer, 285  
 in tuberculosis, 286  
 in typhoid fever, 288  
 meat, 285, 286  
 relation of, to endurance, 284

Digestion in intestines, 21  
 Digestive ferments, 42  
   value of mixtures of, 43  
   tract, diseases of, 17  
   physiology of, morbid, 22  
   normal, 17  
 Digitalis, 289  
   arrhythmia from, 291  
   in aortic incompetence, 291  
 Digitoxin, 290  
 Dilatation of colon, idiopathic, 92  
 Diphtheria, 262  
 Dropsy, cardiac, 325  
 Dysentery, 266  
 Dysmenorrhea, 308  
 Dyspepsia, intestinal, 90, 91

**E**

ECLAMPSIA, 304  
 Electricity, 292  
 Elephantiasis, 212  
 Enchondroma, 220  
 Endurance and diet, 284  
 Eneuresis, nocturnal, 271  
 Enteroptosis, 64  
 Eosinophilia in intestinal disease, 88  
 Epididymitis, 247, 250  
   gonorrheal, 255, 321  
   sulphate of magnesium for, 255  
 Epilepsy, 279  
 Epiphyseal separation of lower end of  
   femur, 171  
 Epithelial tumors, 196-202  
 Epithelioma, adamantine, 218  
 Erysipelas, 309, 321  
 Esophagus, peptic ulcer of, 61  
 Ether anesthesia, 148  
 Ethyl chloride anesthesia, 147  
 Exercise, 294  
 Exophthalmic goitre, 250, 285  
 Exostosis bursata, 220  
 Extirpation of bladder, 237  
 Extremities, tumors of, 194

**F**

FAT-SPLITTING ferment in gastric juice, 19  
 Fats, intolerance of, 38  
 Fecal bacteria, estimation of, 79  
 Feces, lost albumin in, 90  
   occurrence of, 90  
   recognition of, 90  
 Femur, epiphyseal separation of lower  
   end of, 171  
   fracture of neck of, 161-167  
   healing of, 164  
   non-union in, 166  
   operative treatment of, 166  
 Fermentation, intestinal, 70  
 Fever in cancer, 49  
 Fibroma, 209  
   medullary, 218  
   molluscum, 213  
   periosteal, 220  
 Fingers, ganglion of, 210

Foods, medicinal, 282  
 Foodstuffs, antiseptics for, 22  
 Fractures, 148  
   Bier's hyperemia for, 150  
   compound, 155-158  
   functional treatment of, 149  
   glycosuria after, 159  
   injury of vessels in, 159  
   mechanism of, 158  
   obstruction of artery due to kinking  
     in, 160  
   of femur, neck, 161-167  
     shaft, 169-171  
   of leg, 178  
   of patella, 171-174  
   of pelvis, 161  
   of tibia, beak-shaped process of, 176  
     upper end, 177  
   of trochanter, 169  
   operative treatment of, 153  
   spontaneous, in paralysis, 159  
   x-rays in, 159  
 Fresh air, 295  
   in anemia, 296  
   in hospital wards, 296  
   in insane, 298  
   in pneumonia, 296  
   in pregnancy, 297  
   in puerperal infections, 298  
   in septicemia, 296  
   in tuberculosis, 298  
   in typhoid fever, 296, 298

**G**

GALL-BLADDER in gallstone disease, 102  
 Gallstones and biliary infections, 97  
   discharge of, 106  
   fever in, 102  
   gall-bladder in, 102  
   jaundice in, 101  
   pain in, 100  
   symptoms of, 99  
   treatment of, 104  
 Ganglion of fingers, 210  
   of wrist, 210  
 Ganglioneuroma, 214  
 Gangrene due to phenol, 310  
 Gastralgia, 275  
 Gastric cancer, 275  
   contents, hydrochloric acid in, 65  
   juice, fat-splitting ferment in, 19  
   natural inhibition of, 21  
   secretion of, in human beings, 20  
   pain, 272. *See also* Stomach.  
   ulcer, 275  
 Gastritis, 275  
 Gastro-enterostomy, morbid physiology  
   of, 59  
 Gastro-intestinal disease, significance of,  
   cutaneous hyperesthesia in, 36  
 Gastrotaxis, 55  
 Genito-urinary diseases, 227  
 Giant-celled sarcoma, 219, 224  
 Glycosuria after fractures, 159  
 Gonorrhea, 254

Gonorrhea, effect of, on infants, 254  
   opsonic index in, 255  
   prevalence of, 254  
   serum for, 255  
   treatment of, 255  
   vaccine therapy in, 255  
 Gonorrheal arthritis, 255, 321  
   in children, 184  
   epididymitis, 255, 321  
     magnesium sulphate for, 255  
   peritonitis, 254  
     in moles, 254  
   vesiculitis, 258  
 Gruber-Widal reaction and jaundice, 96  
 Guaiacol, 281  
   carbonate, 281  
 Gymnastics, pulmonary, 294

**H**

HEADACHE, 308  
 Heart disease, 278, 285, 293, 319, 325  
 Hematuria, 120, 129-131, 227  
   adrenalin for, 227  
   due to chlorate of potassium, 229  
   in nephritis, 228  
   in tuberculosis, 229  
 Hemoglobinuria, malarial, 314  
 Hemophilia, 138, 322  
 Hemoptysis, 307  
 Hemorrhage in pancreas, 112  
   treatment of, 135  
 Hepatic colic, 306  
 Hermaphroditism, 251  
 Hernia and cellulitis of spermatic cord, 251  
 High-frequency currents, 292  
   in heart disease, 293  
   in rheumatism, 293  
   in rheumatoid arthritis, 293  
   in tuberculosis, 293  
 Hirschsprung's disease, 92  
 Home treatment of tuberculosis, 298  
 Hormone, 17  
 Hospital wards, fresh air in, 296  
 Human being, gastric juice in, 20  
 Hydremia, 133  
 Hydrochloric acid and intestinal putrefaction, 78  
   new reaction for, in gastric contents, 65  
 Hydronephrosis, 113-118  
   acquired, 115  
   congenital, 113  
   pathology of, 113  
 Hyoscine, 302  
 Hyperacidity, 39, 80  
 Hyperemia, Bier's, 140, 150, 186  
   for fractures, 150  
   for joint infections, 186  
 Hyperesthesia, cutaneous, in gastro-intestinal disease, 36  
 Hypersecretion, alimentary, 65  
 Hypertension, pathology of, 125  
   treatment of, 125  
 Hysteria, 285

**I**

ICHTHYOL, 303  
 Icterus. *See* Jaundice.  
 Impotence, 326  
 Indol, 73  
 Infancy, diarrhea of, 281  
 Infants, effect of gonorrhea, 254  
 Infections, 140  
   of biliary tract, 92  
   of seminal vesicle, 256  
 Influenza, 308, 316  
   arthritis in, 184  
 Intestinal antiseptics, 78, 84, 281  
   bacteria, 68  
     after childhood, 69  
     at birth, 69  
     function of, 68  
     in early life, 69  
     not harmful, 69  
   diseases, eosinophilia in, 88  
   dyspepsia, 90  
   fermentation, 70  
     pathological physiology of, 70  
   obstruction due to persistent urachus, 232  
   origin of chronic auto-intoxication, 67  
   putrefaction, 70  
     and hydrochloric acid, 78  
     aromatic products of, 72  
     basic substances in, 71  
     cadaverin in, 71  
     cresol in, 72  
     indol in, 73  
     pathological physiology of, 70  
     phenol in, 72  
     putrescin in, 71  
     skatol in, 72  
     sulphur compounds in, 71  
     susceptibility to, 73  
     therapeutic considerations in, 76  
     types of, 76  
       combined, 74, 76  
       indolic, 74  
       saccharobutyric, 74, 75  
 Intestines, 67  
   absorption in, 21  
   digestion in, 21  
   effect of drugs on, 28, 85  
   movements of, 27  
   tension in, 18  
 Intra-intestinal tension, 18  
 Intragastric tension, 18  
 Iodide of calcium, 303  
   of potassium, 303  
   diagnostic use of, in tuberculosis, 303  
 Iodine, 304  
 Iron, 305  
 Isoprol, 274

**J**

JAUNDICE, 81  
   and Widal reaction, 96  
   chronic, 108  
     splenic enlargement in, 108, 110  
   in gallstone disease, 101

**Joint infections, 179**

- Bier's hyperemia for, 186
- clinical picture of, 185
- diagnosis of, 185
- due to gonococcus, 184
- etiology of, 182-184
- pathology of, 179-182
- treatment of, 186

**Joints, surgery of, 179**

- tuberculosis of, 187
- anatomical considerations in, 189
- and cold abscess, 191
- and heredity, 188
- and inherited predisposition, 188
- bone involvement in, 190
- cartilage changes in, 190
- caseous foci in, 191
- free fibrin in, 191
- symptoms of, 189
- synovial membrane in, 191

**K****KELOID, 209****Kidney, arteries of, sclerosis of, 121-124**

- congenital transposition of, 231
- diseases of, 227
- extracts, 127
- functional activity of, 131
- movable, 116. *See also Renal.*
- tuberculosis of, hematuria in, 229
- tumors of, in children, 118
  - diagnosis of, 120
  - etiology of, 118
  - hematuria in, 120
  - pathology of, 118
  - symptoms of, 119
  - treatment of, 121

**Kidneys, diseases of, 113**

- arterial tension in, 124

**Knee-joint, internal derangement of, 124****L****LAXATIVES, 78****Lead carbonate, 312**

- poisoning, 306

**Leg, fracture of, 178**

- ulcers, 303, 309

**Lenhartz treatment of gastric ulcer, 285****Leukemia, priapism in, 252****Light, physiological action of, 301****Lipoma, 215**

- osteoperiosteal, 221

**Litholapaxy, 239****Liver, 92****Local anesthesia, 146****M****MALARIA, 312**

- pernicious, 313

**Malarial hemoglobinuria, 314****Mechanism of fractures, 158****Medicinal foods, 282****Medullary fibroma, 218****Menopause, premature, 327****Mett's method of estimating pepsin, 24****Moles, congenital pigments, 205****Morphine, 306****Mumps, orchitis in, 249****Myoma, 215****Myxedema, 321****Myxochondroma, 220****Myxoma, 219****N****NASAL irritation a cause of priapism, 252****Necrosis of pancreas, 112****Nephritis, 276**

- hematuria in, 228

- interstitial, 121

- scarlatinal, 273, 292

- toxic and surgical lesions, 231

**Neuralgia, 260, 308****Neurasthenia, 285****Neuritis, 260, 285, 321****Nevi, congenital, 207****Nitrite of amyl, 307****Nitrous oxide anesthesia, 244****Novaspirin, 308****O****OBSTETRICS, scopolamine-morphine**

- anesthesia in, 302

**Occult blood, new tests for, 51****Esophagus. *See* Esophagus.****Operative treatment of fractures, 153****Opeonic index in gonorrhea, 255****Orchitis in mumps, 249**

- in tonsillitis, 249

- in typhoid fever, 249

**Osteomyelitis, 309**

- purulenta tuberculosa, 193

**Osteoperiosteal lipoma, 221****Osteosarcoma, periosteal, 220****Ovary, internal secretion of, 250****Oxaluria a cause of urethral irritation, 253****Oxygen for cystoscopy, 239**

- for radiography, 239

**P****PAIN, visceral, morbid physiology of, 31****Pancreas, 112**

- hemorrhage in, 112

- pathogenesis of, 112

- necrosis of, 112

- pathogenesis of, 112

**Paralysis, spontaneous fractures in, 159****Patella, fractures of, 171-174****Pelvis, fractures of, 161****Pepsin, 42**

- Mett's method of estimating, 24

**Peptic activity, increase of, 23**

- inhibition of, 22

- ulcer of esophagus, 61

**Perineal prostatectomy, median, 241****Periosteal fibroma, 220**

Periosteal osteosarcoma, 220  
 Peritonitis, gonorrheal, 254  
     in moles, 254  
     tuberculous, 301  
 Permanganate of potassium, 261  
 Phenol, 305, 308  
     gangrene, 310  
     in intestinal putrefaction, 72  
     poisoning, 308  
 Phlebotomy, 325  
 Physostigmine, 127  
 Picric acid, 310  
 Pneumonia, 296, 297  
 Poisoning, chloral, 275  
     lead, 306  
     phenol, 308  
 Portal pressure in portal cirrhosis, 110  
 Postoperative suppression of urine, 319  
     treatment of, 307  
 Pregnancy, complications of, 297  
 Priapism, 252  
     due to leukemia, 252  
     due to nasal irritation, 252  
 Prostate, 239  
     cancer of, 244  
     enlarged, 241-244  
     sarcoma of, 241  
     x-rays for, 241  
 Prostatectomy, perineal, median, 241  
     suprapubic, 243  
 Prostatitis, chronic, 239  
     and colon bacillus, 239  
     and infections, 239  
     operative treatment of, 240  
 Pseudarthroses, 151  
 Puerperal period, 298  
 Pulmonary gymnastics, 294  
 Pus tubes in the male, 256  
 Putrefaction, intestinal, 70  
 Putrescin, 71

## Q

QUININE, 312  
     hydrochloride of, 312  
     hypodermic injection of, 312  
         tetanus after, 313, 314  
     to stimulate uterine contractions, 316  
     use of, in children, 314

## R

RADIOGRAPHY, oxygen for, 239  
 Renal colic, 230, 306  
     due to an anomalous artery, 230  
     extract, 127  
     hematuria, 120, 129, 227  
     pain and appendicular affection, 230.  
     *See also* Kidney.  
 Rheumatism, 285, 293, 317, 321  
 Rheumatoid arthritis, 238  
 Rupture of bladder, 238

## S

SAHLI's desmoid reaction, 26  
 Salicylate of bismuth, 87

Salicylate of sodium, 317  
     untoward effects of, 318  
 Sarcoma, 279  
     giant-celled, 219, 224  
     of scar tissue, 211  
 Scar tissue, sarcoma of, 211  
 Scarlatinal nephritis, 292  
 Scarlet fever, 273  
     arthritis in, 184  
 Sciatica, 261  
 Scopalamine, 302  
     morphine anesthesia, 144, 302  
 Seasickness, 275  
 Seminal vesicle, infections, 256  
     removal of, in genital tubercu-  
     losis, 248  
 Septicemia, 296  
 Shock, 135  
 Skatol, 72  
 Skin, cancer of, 197  
 Snake bites, 261  
 Solamon's test for gastric cancer, 47  
 Somnos, 274  
 Sparteine, 318  
 Spermatic colic, 230  
     and appendicitis, 230  
     cord, cellulitis of, 251  
     fluid, 251  
     detection of, 251  
 Spermatocoeles, 251  
 Spinal anesthesia, 145  
 Splenic enlargement in jaundice, 108  
 Splenomegaly, acholuric icterus with, 110  
 Sprained ankle, 321  
 Starch digestion, 81  
 Sterility, 250  
     due to epididymitis, 250  
     due to stenosis of vas, 250  
     due to x-rays, 250  
     operative treatment of, 250  
 Stomach, 17  
     cancer of, 37, 43  
     and ulcer, 49  
     blood in, 46  
     diagnosis of, 43, 50  
     fever in, 49  
     loss of weight in, 47  
     predisposing causes of, 44  
     secondary, 51  
     Solamon's test for, 47  
     symptoms of, 44, 45, 48  
     treatment of, 50  
     x-rays for diagnosis of, 50  
     contents, new test for HCl in, 65  
     effect of alcohol on, 29  
     of drugs on, 28  
     mechanism of, 17  
     movements of, 27  
     oozing of blood from, 55  
     tension in, 18  
     ulcer of, 55, 285  
         cure of, 57  
         diet in, 285  
         effect of aerophagia on, 58  
         pathogenesis of, 55  
 Stone in bladder, 239  
     litholapaxy for, 239

Strophanthin, 319  
 Strophanthus, 319, 290  
 Sulphate of magnesium, 319  
     anesthesia from, 319  
     for epididymitis, 255  
 Sulphur compounds in intestines, 71  
 Suprapubic prostatectomy, 244  
 Surgery of bloodvessels, 135, 139  
     of extremities, 135  
     of joints, 179  
 Surgical physiology, 135  
     tuberculosis, 301  
 Suture of bloodvessels, 135  
 Syphilis, 247  
 Syphilitic arthritis, 184  
     necrosis, 303

**T**

TASTE, subjective, disturbance of, 27  
 Testicle, tumors of, 247  
 Testicles, 245  
     internal secretion of, 250  
     torsion of, 250  
     traumatic injury of, 249  
         damages for, 249  
     tuberculosis of, 245  
         age, 245  
         conclusion on, 248  
         diagnosis of, 247  
         exciting causes of, 246  
         extirpation of vas and seminal  
         vesicles for, 248  
         onset of, 246  
         predisposing causes, 245  
 Tetanus, 267, 313, 314, 320  
 Therapeutic referendum, 259  
 Thyroid extract, 321  
 Tibia, fracture of beak-shaped process  
     of, 176  
     of upper end of, 176  
 Tonsillitis, orchitis in, 249  
 Tonsils, portals of infection, 182  
 Torsion of testicle, 250  
 Transfusion of blood, 135  
 Trauma and sarcoma, 204  
 Treatment of actinomycosis, 304  
     of alcoholism, acute, 270  
     of anemia, 296, 305  
     of angina pectoris, 303  
     of arteriosclerosis, 304  
     of arthritis, gonorrheal, 321  
     of asthenia, 306  
     of bradycardia, 278  
     of buboes, 309  
     of burns, 310  
     of carcinoma of stomach, 50, 275  
     of chancres, 309  
     of contusions, 321  
     of coryza, 316  
     of diabetes mellitus, 288  
     of diabetic coma, 289  
     of diarrhea of childhood, 281  
         of infancy, 281  
     of diphtheria, 262  
     of dropsy, cardiac, 325

Treatment of dysmenorrhea, 308  
     of eclampsia, 304  
     of enuresis, nocturnal, 271  
     of epididymitis, gonorrheal, 255, 321  
     of epilepsy, 279  
     of erysipelas, 309, 321  
     of exophthalmic goitre, 250, 285  
     of fractures, 148  
     of gall-bladder infections, 106  
     of gallstones, 104  
     of gastralgia, 275  
     of gastric cancer, 275  
         pain, 272  
         ulcer, 275, 285  
     of gastritis, 275  
     of headache, 308  
     of heart disease, 278, 285, 289, 293,  
         319, 325  
     of hemophilia, 322  
     of hemoptysis, 307  
     of hemorrhage, 135  
     of hypertension, 125  
     of hysteria, 285  
     of impotence, 326  
     of infections, 140  
     of inflammation of vas, 251  
     of influenza, 308, 316  
     of intestinal dyspepsia, 91  
         putrefaction, 76  
     of leg ulcers, 303, 309  
     of malaria, 312  
     of menopause, premature, 327  
     of myxedema, 321  
     of nephritis, 276  
         scarlatinal, 292  
     of neuralgia, 260, 308  
     of neurasthenia, 285  
     of neuritis, 260, 285, 321  
     of osteomyelitis, 309  
     of peritonitis, tuberculous, 301  
     of pneumonia, 296, 297  
     of postoperative suppression of urine,  
         319  
     of pregnancy, complications of, 297  
     of referred pain, 260  
     of renal colic, 306  
         tumors, 121  
     of rheumatism, 285, 293, 317, 321  
     of rheumatoid arthritis, 293  
     of sarcoma, 279  
     of scarlet fever, 273  
     of sciatica, 261  
     of seasickness, 275  
     of seminal vesicle infections, 256  
     of septicemia, 296  
     of shock, 135  
     of snake bites, 261  
     of spasm of cervix uteri, 306  
     of sprained ankles, 321  
     of syphilitic necrosis, 303  
     of tetanus, 320  
     of tuberculosis, 281, 286, 293, 294,  
         298, 301  
     of tumors, malignant, 322  
     of tympanites, 288, 324  
     of typhoid fever, 288, 296, 298, 305  
     of ulcer of bladder, 234

Treatment of ulcer of stomach, 55,  
285  
of uremia, 127  
of uterine hemorrhage, 281, 308  
of vomiting, 306  
of whooping-cough, 273  
of wounds, 269  
Trochanter, fractures of, 169  
Trypsin, 322  
Tuberculin, 237  
Tuberculosis, 281, 293, 294, 303  
diet in, 286  
home treatment of, 298  
of bladder, 236  
tuberculin for, 237  
of bone, 192  
healing of, 193  
infiltrating, 193  
x-rays in diagnosis of, 194  
of joints, 187  
anatomical consideration in, 189  
and cold abscess, 191  
and heredity, 188  
and inherited predisposition,  
188  
bone involvement in, 190  
cartilage changes in, 190  
caseous foci in, 191  
free fibrin in, 191  
symptoms of, 189  
synovial membrane in, 191  
of testicles, 245  
age, 245  
conclusions on, 248  
diagnosis of, 247  
exciting causes of, 246  
extirpation of vas and seminal  
vesicles for, 248  
onset of, 246  
predisposing causes, 245  
renal, hematuria in, 229  
surgical, 301  
Tuberculous peritonitis, 301  
Tumors, 194, 322  
bone, 215-225  
connective tissue, 202-215  
epithelial, 196-202  
malignancy of, 195, 235  
of extremities, 194  
of kidney in children, 118  
diagnosis of, 120  
etiology of, 118  
hematuria in, 120  
pathology of, 118  
symptoms of, 118  
treatment of, 121  
of testicle, 247  
Turpentine, 288, 324  
Tympanites, 288, 324  
Typhoid fever, 288, 296, 305  
orchitis in, 249  
infection of biliary tract, 95  
different forms of, 96  
Gruber-Widal reaction  
in, 96  
relation of relapses to,  
96

## U

ULCER, carcinomatous, 49  
of bladder, 233  
acute perforating, 233  
diagnosis of, 234  
prognosis of, 234  
treatment of, 234  
of stomach, 55, 275, 285  
cure of, 57  
diet for, 285  
effect of aërophagia on, 58  
pathogenesis of, 55  
peptic, of esophagus, 61  
Urachus, 232  
cysts of, 232  
intestinal obstruction due to a per-  
sistent, 232  
Uremia, 127  
Ureter, 231  
implantation of, in bladder, 232  
occlusions of, 231  
Urethral irritation due to oxaluria, 253  
Urine, postoperative suppression of, 319  
Uterine contractions, quinine for, 316  
hemostatic, 281, 308

## V

VACCINE therapy for gonorrhea, 255  
Vas deferens, removal of, in genital tuber-  
culosis, 248  
stenosis of, 250, 251  
Venesection, 325  
Veronal, 326  
Vesiculitis, gonorrheal, 258  
Vesiculotomy for cystitis, 257  
Vessels, suture of, 135, 139  
Viscera, abdominal, effect of cocaine on,  
32  
external stimuli on, 34  
Visceral pain, physiology of, 31  
Vomiting, 306  
physiology of, 27

## W

WEIL's disease, 97  
Whooping-cough, 273  
Widal reaction and jaundice, 96  
Wounds, treatment of, 269  
Wrist, ganglion of, 210

## X

X-RAY sterility, 250  
X-rays for diagnosis of gastric cancer, 50  
for enlarged prostate, 241  
in bone tuberculosis, 194  
in fractures, 159

## Y

YOHIMBIN, 326

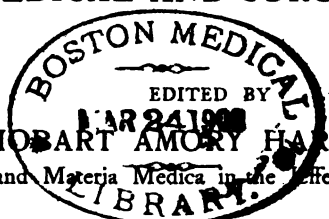


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